“Novel Metal-Free Method for aryl chalcogenation of olefin”

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“Novel Metal-Free Method for aryl chalcogenation of olefin”

A THESIS

Submitted in partial fulfillment of the requirements for the award of the degree of

Master of Science

by

Varsha Kumari

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DEPARTMENT OF CHEMISTRY

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CANDIDATE'S DECLARATION

I hereby certify that the work being presented in the thesis entitled **"Novel Metal-Free Method for aryl chalcogenation of olefin"** in the partial fulfillment of the requirements for the award of the degree of MASTER OF SCIENCE and submitted to the Department of Chemistry, Indian Institute of Technology Indore, is an authentic record of my work carried out during the period from July 2023 to May 2024 under the supervision of Dr. Umesh A. Kshirsagar, Associate Professor, Department of Chemistry, IIT Indore.

Varsha

Varsha Kumari

19.05.2025

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Varsha Kumari has successfully given her M.Sc. Oral Examination held on 16/05/25.

19.05.2025

Signature of Supervisor of M.Sc. thesis
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19.05.2025

Convener DPGC
Dr. Umesh
Date:

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Varsha Kumari

M.Sc. 2nd Year

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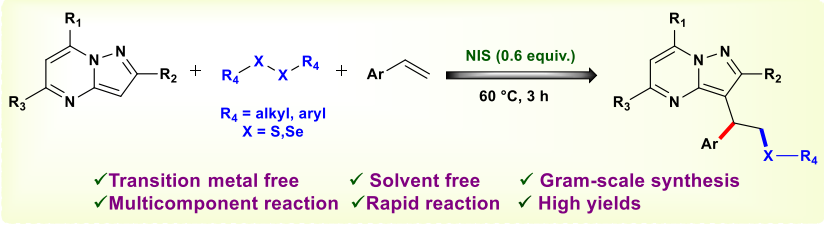
ABSTRACT



N-iodosuccinimide (NIS) mediated transition metal and solventfree, regioselective multicomponent cascade reaction is developed for the C-3 alkylation of pyrazolo[1,5-*a*]pyrimidines via a three-component reaction of styrenes, diaryl dichalcogenides and pyrazolo[1,5-*a*]pyrimidines. This operationally simple, costeffective and rapid reaction furnishes C-3 functionalized pyrazolo[1,5-*a*]pyrimidines in good to excellent yields. The reaction is scalable and operates via an electrophilic substitution mechanism.

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ACRONYMS

^{1}H NMR	Proton nuclear magnetic resonance
^{13}C NMR	^{13}C nuclear magnetic resonance.
ACN	Acetonitrile.
NFSI	N-Fluorobenzenesulfonimide.
PIFA	[Bis(trifluoroacetoxy)iodo]benzene.
DMF	Dimethylformamide
DMSO	Dimethyl sulfoxide
NIS	N-Iodosuccinimide
NBS	N-Bromosuccinimide
NCS	N-Chlorosuccinimide

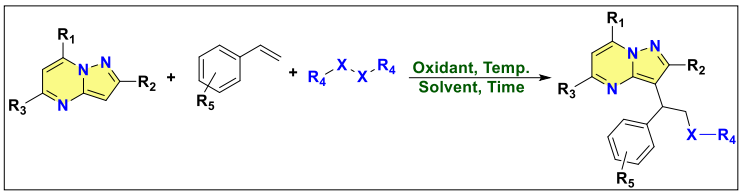
NOMENCLATURE

equiv.	equivalent
mmol	millimole
mg	milligram
h	hour
rt	room temperature
°C	Celsius
mL	millilitre
δ	chemical shift

Chapter 1 - INTRODUCTION

1.1. OBJECTIVE

A novel and synthetic method for C-H functionalization of key heterocycles is an area of significant focus, particularly in alignment with the principles of green chemistry. We aim to enhance reaction efficiency while effectively addressing environmental and economic concerns. We aim to achieve regioselective C3 alkylation of pyrazolo[1,5-*a*]pyrimidines using styrene, diphenyl diselenide, and a mild oxidant. The formation of these C-C and C-X bonds will be accomplished through either (a) a radical pathway or (b) an ionic pathway.



Scheme 1 -General scheme of our work.

1.2. MOTIVATION

The pyrazolo[1,5-*a*]pyrimidine scaffold stands out as a pivotal structure, attracting considerable attention due to its vast array of pharmacological and biological activities.[1] In pharmaceutical industries, this context is highly regarded for its potent anti-tumour, antiviral, anticancer, anti-malarial, and anti-inflammatory properties. Its presence in anti-cancer drugs like repotrectinib, selitrectinib and larotrectinib, as well as in insomnia treatments like zaleplon and lorediplon, highlights the therapeutic importance of pyrazolo[1,5-*a*]pyrimidine as a core unit (Fig 1).[2] Additionally, beyond its medicinal applications, this particular core shows significant potential in materials science, where it is being investigated for its optical properties and chemo-sensor abilities.[3]

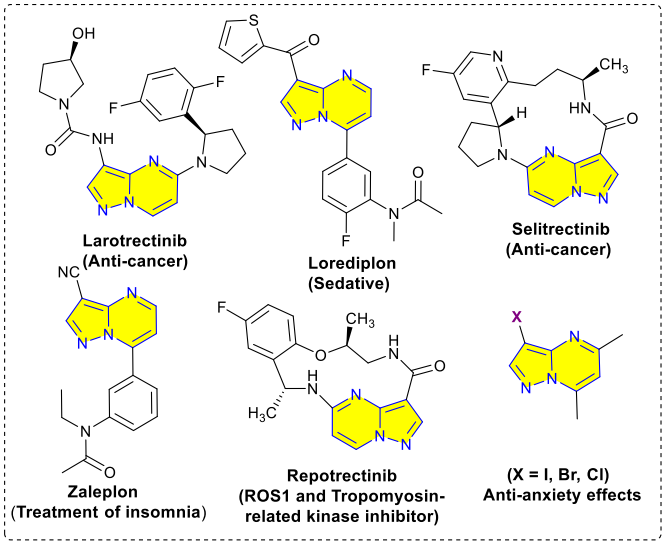


Fig. 1 – Biological compounds with pyrazolo[1,5-a]pyrimidine.

The C–H bond functionalization is a significant advancement in synthetic methodology, facilitating innovative retrosynthetic disconnections and crucial C–C bond formation. By using C–H bonds as functional handles instead of pre-functionalized substrates, this method reduces step counts in synthesis and improves atom economy.[4] In recent years, C–H activation has evolved into a practical and efficient approach for the synthesis of complex molecules.

The electrophilic addition of unsaturated substrates, like alkenes or alkynes, through a seleniranium ion intermediate has emerged as a highly effective and versatile strategy for synthesizing complex structures. This strategy enables the simultaneous introduction of a selanyl group and an additional functional group. The direct conversion of alkenes into various organoselenium compounds through three-component reactions is particularly appealing. Subsequently, several efforts have been devoted to developing simplistic and reliable methods for installing a selanyl group into organic outlines.[5] Recent advancements in organochalcogen chemistry underscore the outstanding applications in synthetic organic, medicinal chemistry, agrochemicals, catalysis and their possible properties in materials science. [6-9] Interest is growing in

developing innovative techniques for synthesising compounds containing C–Se bonds. Of all the methods investigated, selenofunctionalization of unsaturated bonds is considered one of the most direct and efficient methods for producing vicinally functionalized selenides. This methodology allows for the simultaneous insertion of selenium functional groups along with other valuable functionalities across the π system, ensuring high atom efficiency.

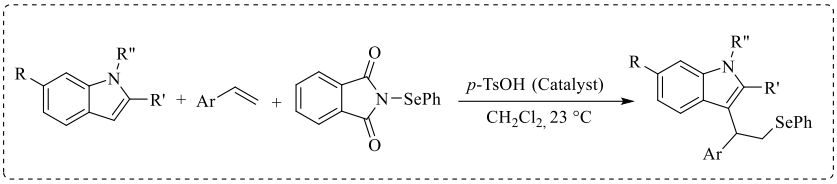
As multicomponent reactions offer a streamlined approach for the synthesis of structurally varied and complex molecules from multiple reactants via one-pot reaction we are using pyrazolo[1,5-*a*]pyrimidines using styrene, diphenyl diselenide, and oxidant for C3 alkylated product. These compounds are gaining attention due to their significant potential across various research fields, including materials science, pharmaceuticals, and organic chemistry. Exploring new synthesis methods leads to the discovery of unique properties and applications for these versatile compounds. [10-18]

1.3. Literature survey

Previous work

C3 alkylation

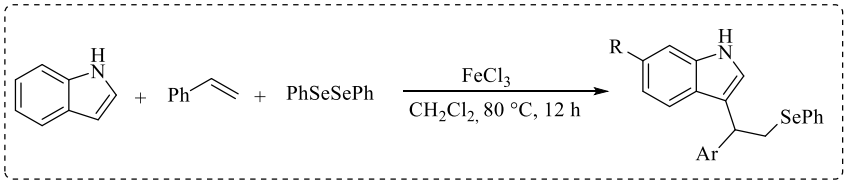
a) Yu's research group demonstrated Brønsted acid (*p*-TsOH) as a catalyst to drive both inter- and intramolecular Friedel−Crafts alkylations and this method was applied for the synthesis of selenated indole derivatives via a three-component coupling and cyclization process. They are using solvent here for carboselenylation reaction. Also, their substrate scope is limited to carboselenylation not sulfenylation. [19]



Scheme 2 - C3 Alkylation of substituted indole.

Zhao, X. D.; Yu, Z. K.; Xu, T. Y.; Wu, P.; Yu, H. *Org. Lett.* **2007**, *9*, 5263–5266.

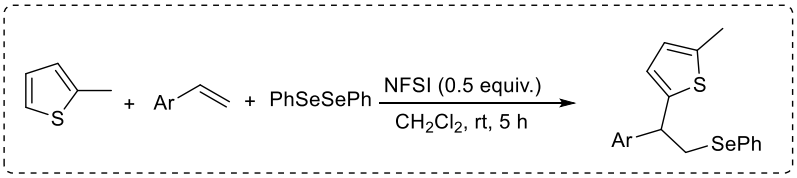
b) Yin's group have reported a three-component aryl-selenylation of alkenes catalyzed by $FeCl_3$, achieving good to excellent yields. However, since diphenyl diselenide has lower reactivity, this reaction requires heating to 80 °C to proceed smoothly. But they used metal-based catalyst for the reaction to perform. Alternatively, they did the reaction using solvent for long hours. [20]



Scheme 3 - C3 Alkylation of substituted indole using $FeCl_3$.

Xu, C.; He, Z.; Yang, H.; Chen, H.; Zeng, Q. *Tetrahedron* **2021**, *91*, 132239.

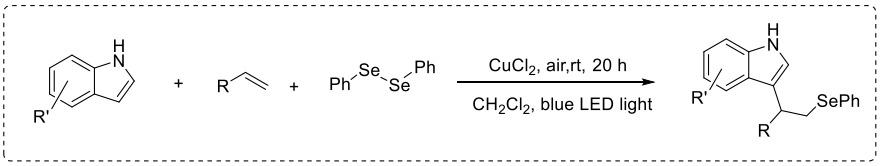
c) Liu's group further developed intermolecular carboselenenylation of olefin using diselenides and N-fluorobenzenesulfonimide (NFSI) under mild, metal-free conditions, offering an efficient pathway for this transformation. They not only used NFSI as their costly oxidant but this reaction only yielded 16% yield for the indole substrate, that is, N-acetyl protected indole. [21]



Scheme 4 - C3 Alkylation of substituted indole using NFSI.

Jiang, Y. Q.; Wang, Y. H.; Zhou, C. F.; Zhang, Y. Q.; Ling, Y.; Zhao, Y.; Liu, G. Q. *J. Org. Chem.* **2022**, 87, 14609–14616.

d) Yin's group disclosed irradiation of blue LED light of a three-component reaction of olefins, indoles, and diaryl diselenides catalysed by $CuCl_2$. The major drawback is they did metal catalysed reaction also using solvent and the reaction time is so long. [22]



Scheme 5 - C3 Alkylation of substituted indole using $CuCl_2$.

Yin, X., Wang, H., Shen, L., & Zeng, Q. *Applied Organometallic Chemistry.*, **2023**, *37*(10), e7231.

1.4 Scope of the Proposed Work

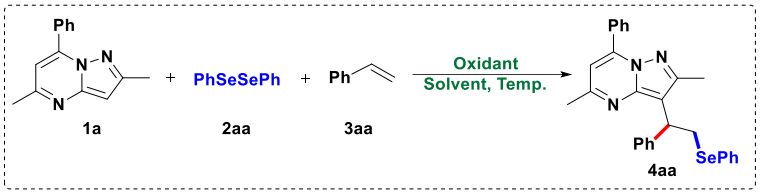
We aim to develop an eco-friendly, sociable and effective method for the regio-selective C3 alkylation of pyrazolo[1,5-*a*]pyrimidines via a three-component reaction involving styrene, diselenide, a low-cost oxidant, and a green solvent, all conducted at ambient temperature. Our goal is to facilitate clean and effective C-C as well as C-Se bond formation, ultimately resulting to the synthesis of a variety of C3-alkylated pyrazolo[1,5-*a*]pyrimidine derivatives. This work will focus on promoting sustainable synthetic methodologies while broadening the scope of functionalized heterocycles.

Chapter 2 - RESULT AND DISCUSSION

To start our investigation, we choose substituted pyrazolo[1,5-*a*] pyrimidine (**1a**), substituted diselenides (**2aa**), substituted styrene (**3aa**) and the results are summarized in Table 1

2.1. REACTION OPTIMIZATION

Table 1- Optimization table[a]



Scheme 6 - C3 Alkylation of substituted pyrazolo[1,5-a]pyrimidine.

Sr No.	Oxidant (equiv.)	Solvent	Yield[b] (%)
1	$K_2S_2O_8$ (1.0)	ACN	16
2	PIFA (1.0)	ACN	42
3	Selectfluor (1.0)	ACN	51
4	I_2 (1.0)	ACN	31
5	NFSI (1.0)	ACN	43
6	NBS (1.0)	ACN	22
7	NCS (1.0)	ACN	NR
8	NIS (1.0)	ACN	72
9	NIS (1.0)	DMSO	16
10	NIS (1.0)	H_2O	21
11	NIS (1.0)	PEG-400	Trace
12	NIS (1.0)	-	89
13	**NIS (0.6)**	**-**	**88**
14	NIS (0.5)	-	76
15[c]	NIS (0.6)	-	63
16[d]	NIS (0.6)	-	46
17[e]	NIS (0.6)	-	48
18[f]	NIS (0.6)	-	61
19[g]	NIS (0.6)	-	86
20	-	-	NR

[a]Reaction condition: **1a** (0.2 mmol), **2aa** (0.1 mmol), **3aa** (0.50 mmol), 60 °C, 3 h; [b]Isolated yield; [c]2.0 equiv. of styrene was used, [d]1.5 equiv. of styrene was used, [e]Reaction at rt, [f]Reaction at 40 °C, [g]Reaction at 80 °C

In light of its significant chemical and biological relevance, the synthesis of C-H functionalization in N-heterocycles is recognized as a valuable and impactful method. Despite the wide array of methodologies available, certain approaches encounter notable challenges including the utilization of toxic and corrosive substances, as well as the occurrence of reactions at elevated temperatures. However, our work embraces a safe methodology that thrives under mild conditions, showcasing our commitment to solvent-free, moderate temp., and cost-effective reactions.

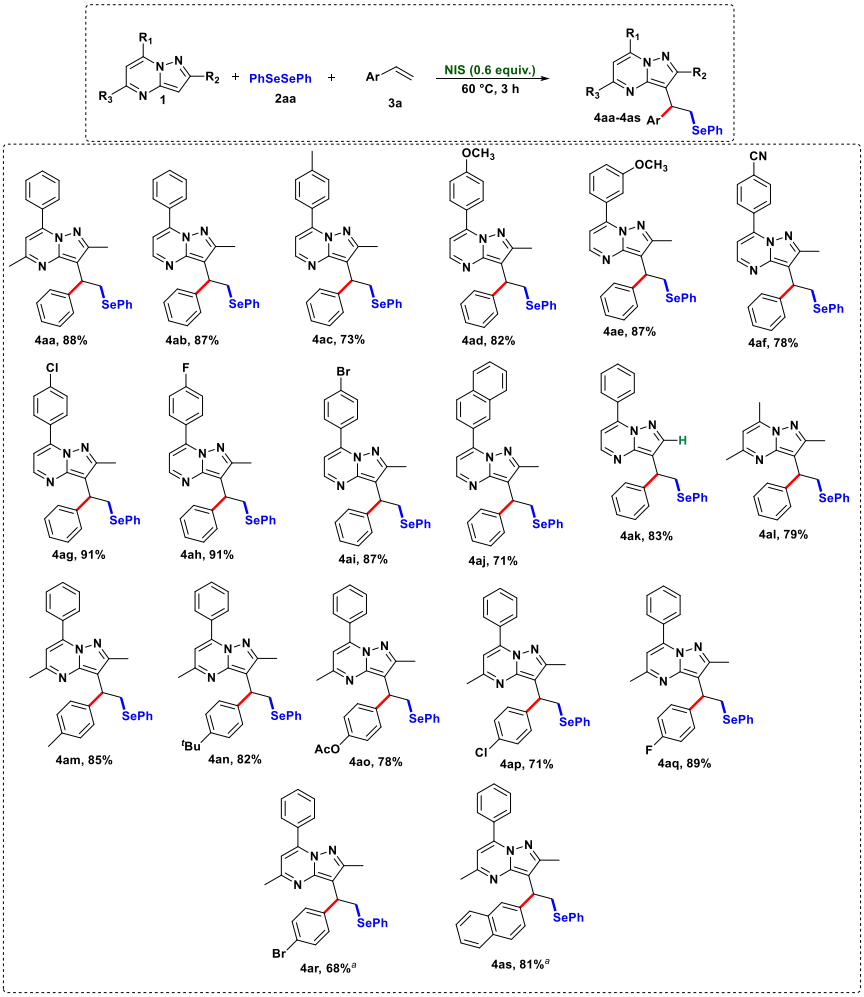
Initially, we chose 2,5-dimethyl-7-phenylpyrazolo[1,5-*a*]pyrimidine (**1a**), diphenyl diselenide (**2aa**) and styrene (**3aa**) as ideal substrates to find out the optimal conditions for the three component carboselenylation reaction. We carried out the reaction of **1a** (1.0 equiv.) with diphenyl diselenide (**2aa**) (0.5 equiv.) and styrene (**3aa**) (2.5 equiv.) in the presence of potassium peroxydisulfate and using acetonitrile as solvent at 60 °C for 3 hours, giving the desired product **4aa** in 16% yield (Table 1, **entry 1**). The isolated product **4aa** was characterized and confirmed by NMR spectroscopy and HRMS analysis. Various oxidants including PIFA, Selecfluor, I_2, NFSI, NBS, NCS and NIS were screened for the carboselenylation reaction as shown in Table 1 (**entries 2-8**). Among all the oxidants, NIS emerged as the most efficient oxidant which provided the product **4aa** in 72% yield and thus, NIS was chosen as the ideal oxidant. Keeping all the other parameters constant subsequent screening of different solvents was done using NIS as an optimal oxidant. DMSO and H_2O afforded lower yields of **4aa** at 16% and 21% (Table 1, **entry 9, 10**) while PEG-400 was ineffective and resulted in only a trace amount of the product **4aa** (Table 1, **entry 11**). Remarkably, carrying out the reaction under solvent-free conditions significantly enhanced the yield achieving product **4aa** in 89% (Table 1, **entry 12**). Further evaluation of the

optimal ratio of NIS under solvent-free conditions revealed that using 0.6 equiv. of NIS yielded 88% of the desired product **4aa** (Table 1, **entry 13**). In contrast, reducing it to 0.5 equiv. led to a little decrease in the yield to 76% (Table 1, **entry 14**). Further decreasing the equivalents of styrene to 2.0 and 1.5 led to a decrease in the yield (63% & 46%) of product **4aa** (Table 1, **entry 15-16**). However, performing the reaction at room temperature and 40 °C yielded moderate outcomes of 48% and 61% respectively (Table 1, **entry 17-18**). When the reaction was carried out at 80 °C, the product **4aa** was obtained in 86% yield (Table 1, **entry 19**). In the absence of NIS, no product formation was observed which confirms the necessity of NIS to carry out the reaction (Table 1, **entry 20**). Thus, the optimized condition for the three-component carboselenylation reaction was determined to be 1.0 equiv. of **1a**, 0.5 equiv. of **2aa**, and 2.5 equiv. of **3aa**, using 0.6 equiv. of NIS under solvent-free conditions at 60 °C for 3 hours, which afforded **4aa** in 88% yield.

2.2. Substrate scope

Substrate scope for various pyrazolo[1,5-*a*]pyrimidines and styrenes was thoroughly carried out. Different substituents, such as electron-donating and electron-withdrawing, resulted in moderate to better yields. With the optimized condition in hand, further investigation of the substrate scope of various pyrazolo[1,5-*a*]pyrimidines was thoroughly carried out (**Scheme 7**). Three-component alkylation of 2-methyl-7-phenylpyrazolo[1,5-*a*]pyrimidine successfully yielded the desired C3 alkylated product **4ab,** achieving a good yield of 87%. Next, 2-methyl-7-phenylpyrazolo[1,5-*a*]pyrimidines bearing electron-donating group (*p*–OMe, *m*–OMe *p*–Me) and electron-withdrawing (*p*–CN) afforded excellent yields with derivatives **4ac-4af** with yields ranging from 73% to 87%. Halogen-substituted 2-methyl-7-phenylpyrazolo[1,5-*a*]pyrimidine (*p*–Cl, *p*–F, *p*–Br) on

the phenyl ring also delivered good yields (87-91%) of the corresponding products **4ag-4ai**. Additionally, 2-methyl-7-(naphthalen-2-yl)pyrazolo[1,5-*a*]pyrimidine smoothly underwent reaction, producing C3 alkylated product **4aj** in 71% yield. Interestingly, the methodology also showcased good regioselectivity while performing the reaction with pyrazolo[1,5-*a*]pyrimidine lacking substituents on the C2 position, exclusively yielding the C3 alkylated product with an impressive 83% yield of the compound **4ak**.



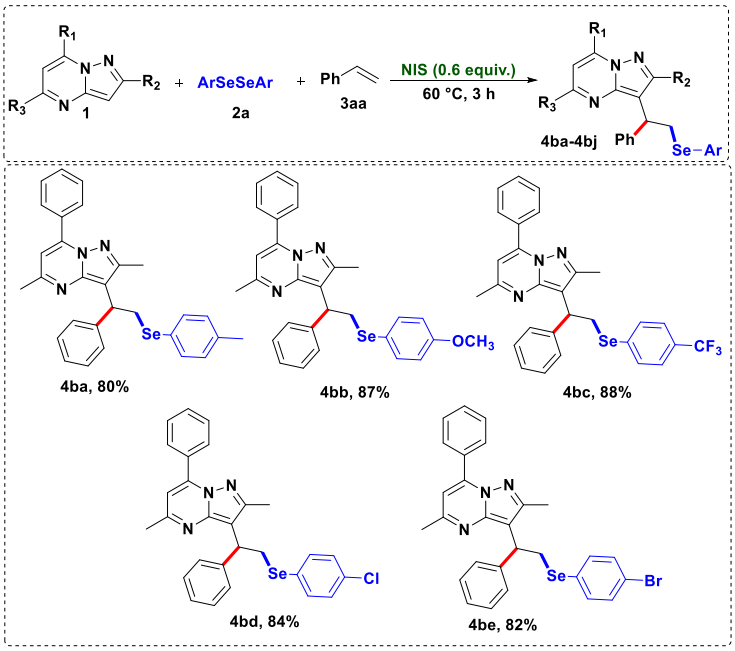
*Scheme 7: Substrate scope for three-component carboselenylation of styrenes. Reaction condition: **1** (0.2 mmol), **2aa** (0.1 mmol), **3a** (0.5 mmol), NIS (0.6 equiv.), 60 °C, 3 h; yields are isolated yields, [a]1.0 mL ACN was used as a solvent.*

Furthermore, 2,5,7-trimethylpyrazolo[1,5-*a*]pyrimidine delivered the desired product **4al** with a yield of 79%. Subsequently, a variety of substituted styrenes were tried for the carboselenylation under the

optimized conditions (**Scheme 8**). Styrenes bearing both electron-donating groups (*p*–Me, *p*–^{t}Bu) and electron-withdrawing group (*p*–$OCOCH_3$) underwent a reaction with 2,5-dimethyl-7-phenylpyrazolo[1,5-*a*]pyrimidine successfully producing regioselective C3 alkylated derivatives **4am-4ao** in yields ranging from 78-85%.

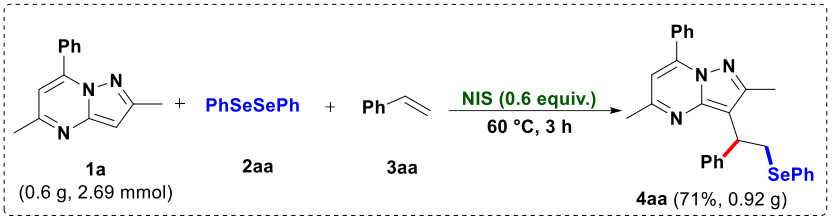
Halogen substituted styrenes also gave a good yield of products **4ap-4ar** in the range of 68-89%. When 2-vinyl naphthalene was used, the corresponding carboselenylated product **4as** was obtained in 81% yield.

Following the exploration of styrenes, a variety of diaryl diselenides were investigated to expand the scope of the reaction as depicted in **Scheme 8**. Various diaryl diselenides having electron donating (*p*–Me, *p*–OMe) and withdrawing group (*p*–CF_3) were successfully introduced achieving consistent yields ranging from 80-88% of products **4ba-4bc**. Halogen substituted (*p*–Cl, *p*–Br) diphenyl diselenides maintained good yields of 78 to 84% of the product **4ba-4be**.



*Scheme 8: Substrate scope for various diorganyl diselenides. Reaction condition: **1** (0.2 mmol), **2a** (0.1 mmol), **3aa** (0.5 mmol), NIS (0.6 equiv.), 60 °C, 3 h.*

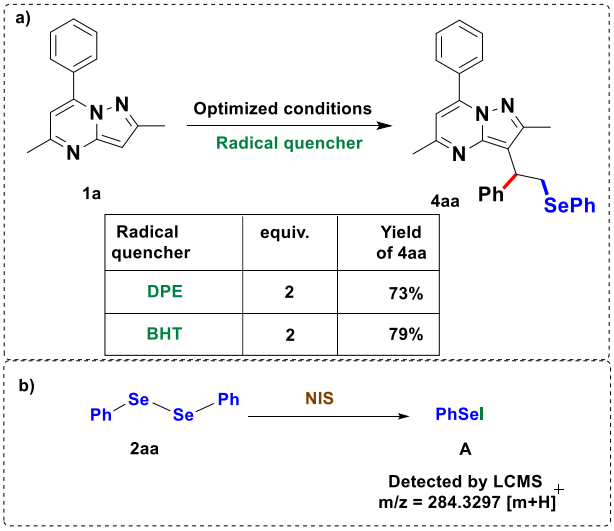
2.3 Scale up reaction for carboselenylation



Scheme 9: Scale-up synthesis for carboselenylation of imidazo[1,2-a]pyridine

Scale up reactions for carboselenylation was done which gives **4aa** with yield 71% demonstrating the robustness and the synthetic utility of the developed protocol serving as precursors for several vital bioactive molecules.

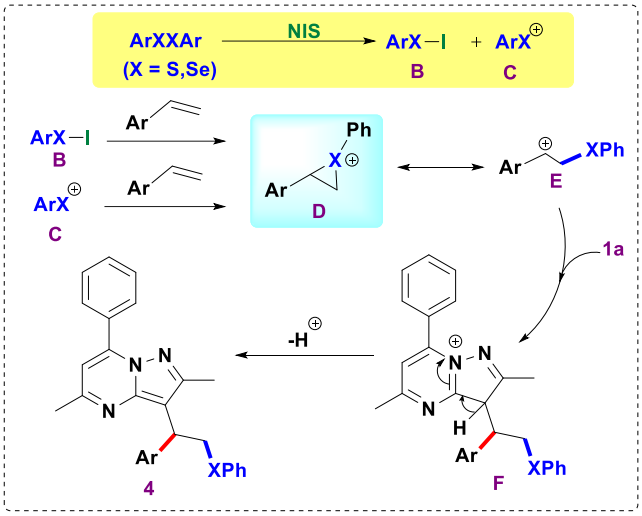
2.4 Control experiments



Scheme 10. *Control Experiments; a) Radical Quenching Experiments b) Intermediate detection.*

To gain further insights into the reaction mechanism, we conducted control experiments. We reacted compound 1a with the radical scavengers, BHT (2,6-di-tert-butyl-4-methylphenol) and 1,1-diphenyl ethylene (DPE). Under these conditions, we observed that the desired carboselenylated product 4aa was obtained in good yield without any significant decrease in the reaction yield thereby ruling out the possibility of radical mechanism.

2.5 Plausible mechanism



Scheme 11. Plausible reaction mechanism

Based on the results of the control experiments and study of literature,[23] we proposed a plausible ionic mechanism for the three component carbochalcogenation reactions (**Scheme 11**). Initially, NIS reacts with diaryl dichalcogenides, forming intermediate **B** and intermediate **C**. Both intermediates **B** and **C** react with styrene to form intermediate **D** and its tautomer intermediate **E**. Subsequently, 2,5-dimethyl-7-phenylpyrazolo[1,5-*a*]pyrimidine (**1a**) reacts with intermediate **E**, leading to the formation of intermediate **F**. In the last step, intermediate **F** undergoes deprotonation to afford the desired product **4**.

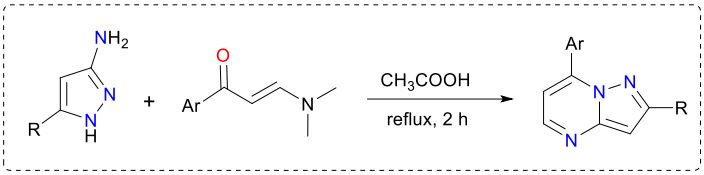
CHAPTER 3: EXPERIMENTAL AND CHARACTERIZATION DETAILS

3.1: Material and instrumentation

All chemicals and reagents that were procured from commercial suppliers (TCI, Spectrochem, BLD pharma) are used without further purification. All reactions were conducted in pre-dried screw cap test tubes made of borosilicate glass. Thin layer chromatography was carried out on aluminium sheets pre-coated with Merck silica gel $60F_{254}$ and visualised under UV light (254 nm). The organic solutions were concentrated using the Heidolph rotary evaporator under reduced pressure. 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 measured with an electrothermal apparatus. All the starting materials and substrates were synthesized according to literature reports.[1,3]

3.2Preparation of starting materials

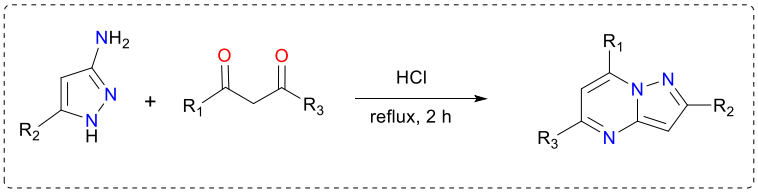
3.2.1 General procedure for the synthesis of substituted pyrazolo[1,5-*a*] pyrimidines.[25a]



Scheme 12: General procedure for the synthesis of substituted pyrazolo[1,5-a] pyrimidines

In an oven-dried round bottom flask (RB), a mixture of substituted amino pyrazoles (1.0 mmol, 1.0 equiv.) and enones (1.0 mmol, 1.0 equiv.) in acetic acid (AcOH) (1.0 mL) was refluxed in an oil bath in stirring condition. The reaction was monitored by TLC analysis. After completing the reaction, the mixture was subjected to extraction using DCM and water. The organic layer was evaporated to obtain the crude pyrazolo[1,5-*a*]pyrimidine derivatives which were purified by column chromatography using 100-200 mesh silica gel and a gradient elution of ethyl acetate-hexane (1:9 to 1:4). Product conformation was done through ^{1}H and ^{13}C NMR spectroscopic analysis.

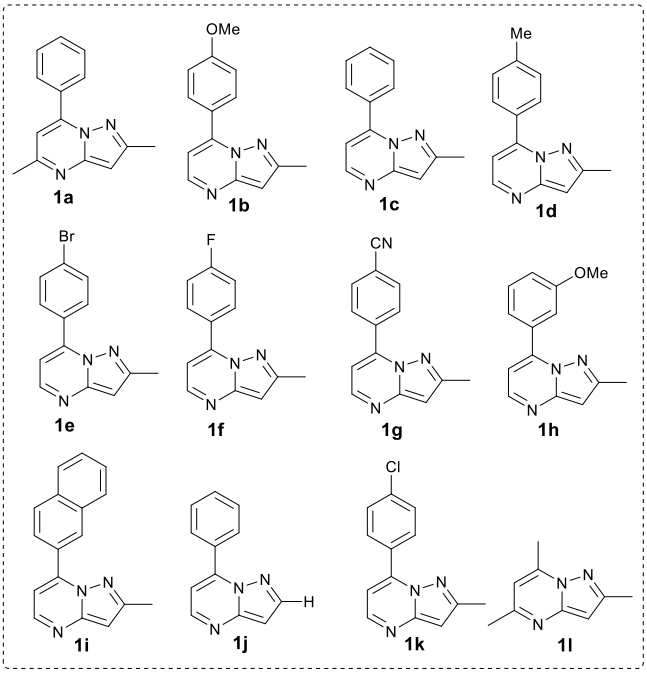
3.2.2 General procedure for the synthesis of substituted pyrazolo[1,5-*a*] pyrimidines.[25b]



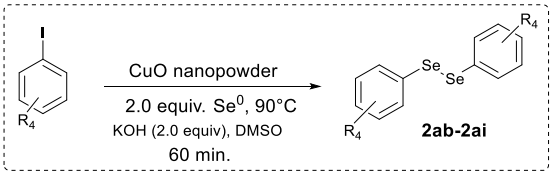
Scheme 13: General procedure for the synthesis of substituted pyrazolo[1,5-a] pyrimidines

In an oven-dried round bottom flask(RB), substituted amino pyrazoles (1.0 mmol, 1.0 equiv.) and diketones (1.0 mmol, 1.0 equiv.) were taken. The reaction mixture was refluxed with vigorous stirring in an oil bath after adding 1.0 mL of HCl. The reaction progress was effectively monitored through TLC analysis. Upon completion of the reaction, the mixture was extracted with

DCM and water. The organic layer was evaporated to obtain the crude pyrazolo[1,5-*a*]pyrimidine derivatives. Product conformation was done through ^{1}H and ^{13}C NMR spectroscopic analysis.

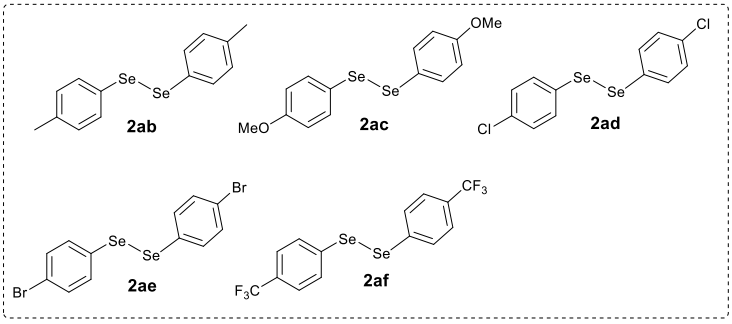


3.2.3 General procedure for synthesis of substituted diselenides:[26]

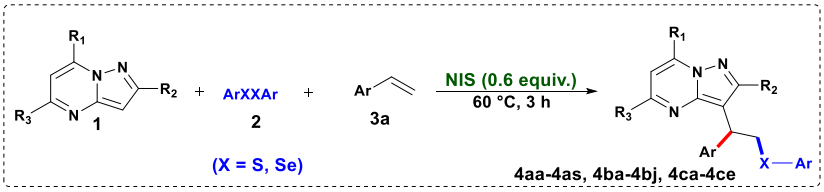


Scheme 14: General procedure for synthesis of substituted diselenides

Under nitrogen atmosphere a solution containing selenium metal (Se^0) (2.0 mmol), copper oxide (CuO) nanoparticles (10.0 mol%) and halides (1.0 mmol) in dry DMSO (2.0 mL) was stirred. Potassium hydroxide (KOH) (2 equiv.) was added. The reaction mixture was heated in an oil bath, and the progress was monitored using TLC. After the reaction was completed, the mixture was cooled and then purified by column chromatography to isolate the desired diselenides. The identity of the products was confirmed through ^{1}H and ^{13}C NMR spectroscopic analysis.



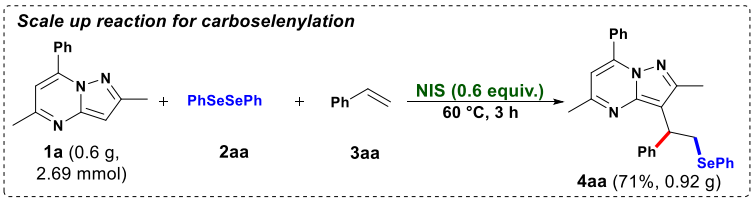
3.2.4: - General experimental procedure for the preparation of C3 alkylated pyrazolo[1,5-*a*]pyrimidine derivatives



Scheme 15: General experimental procedure for the preparation of C3 alkylated pyrazolo[1,5-a]pyrimidine derivatives

In an oven-dried reaction vessel, substituted pyrazolo[1,5-*a*]pyrimidines **1** (0.2mmol, 1 equiv.), diorganyl dichalcogenides **2** (0.1mmol, 0.5 equiv.), substituted styrene **3a** (2.5 equiv.) and NIS (0.6 equiv.) were taken and stirred in an oil bath at 60 °C for 3 hours. Reaction progress was monitored via TLC analysis. After completion, the crude product was purified by silica gel column chromatography (100-200 mesh) to give the desired product. Product confirmation was done using ^{1}H and ^{13}C NMR and HRMS analysis.

3.2.5 Experimental procedure for the scale-up synthesis of 2,5-dimethyl-7-phenyl-3-(1-phenyl-2-(phenylselanyl)ethyl)pyrazolo[1,5-*a*]pyrimidine (4aa):



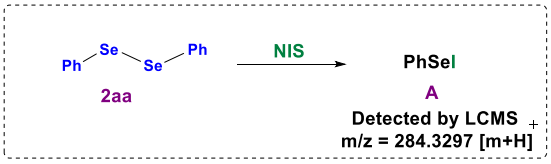
Scheme 16: General experimental procedure for the preparation of C3 alkylated pyrazolo[1,5-a]pyrimidine derivatives

2,5-Dimethyl-7-phenylpyrazolo[1,5-*a*]pyrimidine **1a** (0.6 g, 2.69 mmol), diphenyl diselenide **2aa** (1.34 mmol, 0.5 equiv.), styrene **3aa** (6.72 mmol, 2.5 equiv.) and NIS (0.6 equiv.) were taken and stirred in an oil bath at 60 °C for 3 hours. Reaction progress was monitored via TLC analysis. After completion, the crude product was purified by silica gel column chromatography (100-200 mesh) to give the desired product **4aa** in 71% yield. Product confirmation was done using ^{1}H and ^{13}C NMR and HRMS analysis.

Procedure for control Experiments:

3.2.6 Control experiments for C3 alkylation of pyrazolo[1,5-a]pyrimidines: In an oven-dried reaction vessel, substituted pyrazolo[1,5-*a*]pyrimidines **1aa** (0.2 mmol, 1.0 equiv.), diphenyl dichacogenides **2** (0.1mmol, 0.5 equiv.), styrene **3aa** (0.22 mmol, 2.5-3 equiv.), NIS (0.6 equiv.) and radical scavengers (DPE/ BHT, 2.0 equiv.) were taken and stirred in an oil bath at 60 °C for 3 hours. Reaction progress was monitored via TLC analysis. Product confirmation was done using ^{1}H and ^{13}C NMR and HRMS analysis.

3.2.7 Control experiment for the detection of intermediates involved in selenylation reaction:

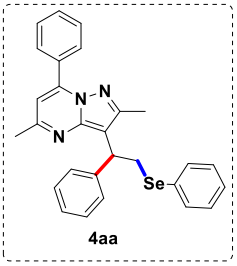


Scheme 17: General procedure for control experiment for the detection of intermediates.

An oven-dried screw-capped test tube was taken with a magnetic stir bar. Diphenyl diselenide (**2aa**) (0.5 equiv., 0.1 mmol), NIS (0.6 equiv.) and ACN (1.5 mL) were added to the test tube. The reaction mixture was stirred at 60 °C for 3 hours. After completion of the reaction, 100µL aliquote of the reaction mixture was taken and diluted with 1.5 mL of MeOH and immediately analyzed using LCMS analysis.

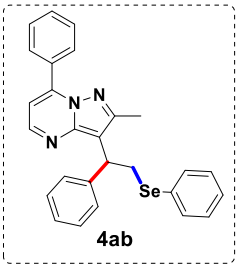
Chapter 4: Supporting data

4.1 Characterization data of compounds (4aa-4as, 4ba-4be):



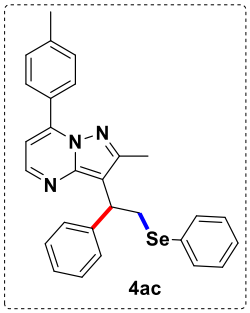
4aa

2,5-Dimethyl-7-phenyl-3-(1-phenyl-2-(phenylselanyl)ethyl)pyrazolo[1,5-*a*]pyrimidine(4aa): Yellow oil; 88% (85 mg); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.91 (q, *J* = 3.7 Hz, 2H), 7.45 (s, 5H), 7.41 – 7.36 (m, 2H), 7.22 (d, *J* = 7.9 Hz, 2H), 7.11 (s, 4H), 6.52 (d, *J* = 3.8 Hz, 1H), 4.37 (d, *J* = 4.3 Hz, 1H), 4.36 – 4.29 (m, 1H), 3.68 (dd, *J* = 11.1, 4.7 Hz, 1H), 2.53 (s, 3H), 2.27 (s, 3H); **^{13}C {^{1}H} NMR** (126 MHz, $CDCl_3$) δ 157.2, 153.1, 147.5, 145.1, 144.8, 133.1, 131.6, 130.7, 130.6, 129.2, 128.7, 128.6, 128.5, 127.8, 126.7, 126.5, 107.9, 107.5, 43.5, 33.1, 25.0, 13.4; **HRMS** (ESI, *m/z*): Calculated for $C_{28}H_{26}N_3Se$ $[M+H]^+$: 484.1288, found 484.1283.

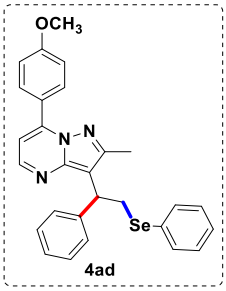


4ab

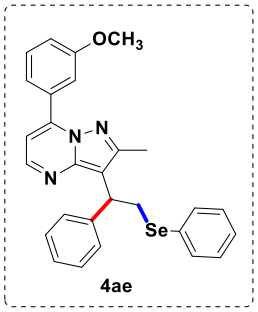
2-Methyl-7-phenyl-3-(1-phenyl-2-(phenylselanyl)ethyl)pyrazolo[1,5-*a*]pyrimidine (4ab): Yellow oil; 87% (81.7 mg); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.32 (d, *J* = 4.4 Hz, 1H), 7.94 (td, *J* = 4.6, 4.1, 2.2 Hz, 2H), 7.47 – 7.41 (m, 5H), 7.40 – 7.34 (m, 2H), 7.23 – 7.19 (m, 2H), 7.14 – 7.07 (m, 4H), 6.67 – 6.61 (m, 1H), 4.41 (dd, *J* = 10.4, 5.6 Hz, 1H), 4.33 – 4.27 (m, 1H), 3.69 (dd, *J* = 11.8, 5.6 Hz, 1H), 2.31 (s, 3H); **^{13}C {^{1}H} NMR** (126 MHz, $CDCl_3$) δ 153.4, 147.7, 145.8, 144.5, 133.0, 131.4, 130.9, 130.4, 129.3, 128.8, 128.7, 128.6, 127.7, 126.7, 126.6, 109.1, 106.5, 43.4, 33.1, 13.4; **HRMS** (ESI, *m/z*): Calculated for $C_{27}H_{24}N_3Se$ $[M+H]^+$: 470.1132, found 470.1132.



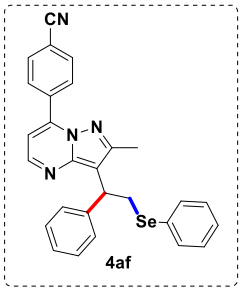
2-Methyl-3-(1-phenyl-2-(phenylselanyl)ethyl)-7-(p-tolyl)pyrazolo[1,5-*a*]pyrimidine (4ac): Orange oil; 73% (72 mg); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.41 (d, *J* = 4.3 Hz, 1H), 7.95 (d, *J* = 8.2 Hz, 2H), 7.51 (d, *J* = 7.2 Hz, 2H), 7.47 – 7.43 (m, 2H), 7.37 (d, *J* = 8.2 Hz, 2H), 7.30 (t, *J* = 7.6 Hz, 2H), 7.23 – 7.16 (m, 4H), 6.74 (d, *J* = 4.3 Hz, 1H), 4.49 (dd, *J* = 10.4, 5.6 Hz, 1H), 4.40 – 4.34 (m, 1H), 3.77 (dd, *J* = 11.9, 5.6 Hz, 1H), 2.46 (s, 3H), 2.40 (s, 3H). **^{13}C {^{1}H} NMR** (126 MHz, $CDCl_3$) δ 153.3, 147.8, 147.7, 146.0, 144.6, 141.3, 133.1, 130.5, 129.4, 129.2, 128.8, 128.6, 128.5, 127.8, 126.7, 126.6, 109.0, 106.2, 43.5, 33.1, 21.6, 13.4; **HRMS** (ESI, *m/z*): Calculated for $C_{28}H_{26}N_3Se$ $[M+H]^+$: 484.1288, found 484.1290.



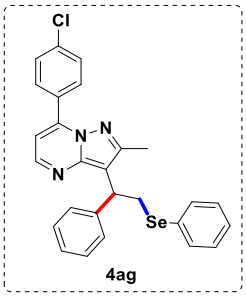
7-(4-Methoxyphenyl)-2-methyl-3-(1-phenyl-2-(phenylselanyl)ethyl)pyrazolo[1,5-*a*]pyrimidine(4ad): Brown oil; 82% (82 mg); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.39 (d, *J* = 4.3 Hz, 1H), 8.06 (d, *J* = 8.9 Hz, 2H), 7.50 (d, *J* = 9.2 Hz, 2H), 7.44 (dd, *J* = 6.6, 3.1 Hz, 2H), 7.29 (t, *J* = 7.6 Hz, 2H), 7.23 – 7.14 (m, 4H), 7.06 (d, *J* = 9.0 Hz, 2H), 6.72 (d, *J* = 4.3 Hz, 1H), 4.48 (dd, *J* = 10.5, 5.6 Hz, 1H), 4.41 – 4.30 (m, 1H), 3.89 (s, 3H), 3.76 (dd, *J* = 11.9, 5.6 Hz, 1H), 2.39 (s, 3H). **^{13}C {^{1}H} NMR** (126 MHz, $CDCl_3$) δ 161.7, 153.22, 147.8, 147.7, 145.6, 144.6, 133.1, 131.0, 130.5, 128.8, 128.6, 127.8, 126.7, 126.6, 123.6, 114.1, 108.9, 105.8, 55.5, 43.4, 33.1, 13.4; **HRMS** (ESI, *m/z*): Calculated for $C_{28}H_{26}N_3OSe$ $[M+H]^+$: 500.1237, found 500.1240.



7-(3-Methoxyphenyl)-2-methyl-3-(1-phenyl-2-(phenylselanyl)ethyl)pyrazolo[1,5-*a*]pyrimidine(4ae): Yellow oil; 87% (86.8 mg); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.38 (d, *J* = 4.3 Hz, 1H), 7.63 – 7.60 (m, 1H), 7.55 – 7.47 (m, 3H), 7.45 – 7.40 (m, 3H), 7.28 (d, *J* = 7.5 Hz, 2H), 7.20 – 7.14 (m, 4H), 7.06 (dd, *J* = 8.2, 3.0 Hz, 1H), 6.71 (d, *J* = 4.3 Hz, 1H), 4.48 (dd, *J* = 10.5, 5.6 Hz, 1H), 4.40 – 4.32 (m, 1H), 3.84 (s, 3H), 3.75 (dd, *J* = 11.9, 5.6 Hz, 1H), 2.38 (s, 3H); **^{13}C {^{1}H} NMR** (126 MHz, $CDCl_3$) δ 159.5, 153.3, 147.7, 147.6, 145.6, 144.5, 133.0, 132.5, 130.3, 129.7, 128.7, 128.5, 127.7, 126.7, 126.6, 121.7, 116.6, 114.8, 109.1, 106.5, 55.4, 43.4, 33.0, 13.4; **HRMS** (ESI, *m/z*): Calculated for $C_{28}H_{26}N_3OSe$ $[M+H]^+$: 500.1237, found 500.1238.

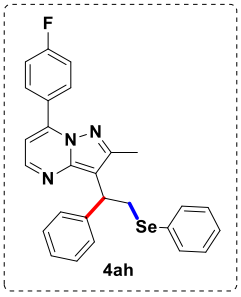


4-(2-Methyl-3-(1-phenyl-2-(phenylselanyl)ethyl)pyrazolo[1,5-*a*]pyrimidin-7-yl)benzonitrile(4af): Orange oil; 78% (77.1 mg); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.42 (d, *J* = 4.3 Hz, 1H), 8.11 (d, *J* = 8.5 Hz, 2H), 7.80 (d, *J* = 8.4 Hz, 2H), 7.42 (d, *J* = 7.9 Hz, 2H), 7.38 (dd, *J* = 6.5, 3.1 Hz, 2H), 7.26 – 7.21 (m, 2H), 7.20 – 7.08 (m, 4H), 6.72 (d, *J* = 4.3 Hz, 1H), 4.42 (dd, *J* = 10.6, 5.4 Hz, 1H), 4.36 – 4.25 (m, 1H), 3.69 (dd, *J* = 11.8, 5.4 Hz, 1H), 2.33 (s, 3H); **^{13}C {^{1}H} NMR** (126 MHz, $CDCl_3$) δ 153.9, 147.6, 144.3, 143.6, 135.7, 133.1, 132.5, 130.2, 130.0, 128.9, 128.7, 127.7, 126.9, 126.8, 118.3, 114.4, 109.8, 106.9, 43.4, 33.1, 13.3; **HRMS** (ESI, *m/z*): Calculated for $C_{28}H_{23}N_4Se$ $[M+H]^+$: 495.1084, found 495.1083.



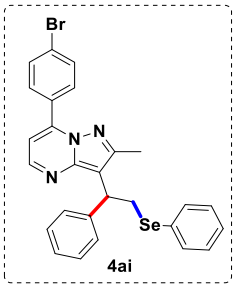
4ag

7-(4-Chlorophenyl)-2-methyl-3-(1-phenyl-2-(phenylselanyl)ethyl)pyrazolo[1,5-*a*]pyrimidine(4ag): Yellow jelly; 91% (91.5 mg); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.33 (d, *J* = 4.4 Hz, 1H), 7.90 (d, *J* = 8.5 Hz, 2H), 7.43 (t, *J* = 7.6 Hz, 4H), 7.39 – 7.31 (m, 2H), 7.24 – 7.18 (m, 2H), 7.17 – 7.02 (m, 4H), 6.62 (d, *J* = 4.6 Hz, 1H), 4.45 – 4.36 (m, 1H), 4.34 – 4.23 (m, 1H), 3.74 – 3.58 (m, 1H), 2.31 (d, *J* = 2.6 Hz, 3H). **^{13}C {^{1}H} NMR** (126 MHz, $CDCl_3$) δ 153.5, 147.7, 147.6, 144.6, 144.5, 137.0, 133.0, 130.6, 130.4, 129.7, 129.0, 128.8, 128.6, 127.7, 126.7, 126.6, 109.3, 106.3, 43.4, 33.0, 13.3; **HRMS** (ESI, *m/z*): Calculated for $C_{27}H_{23}ClN_3Se$ $[M+H]^+$: 504.0739, found 504.0739.

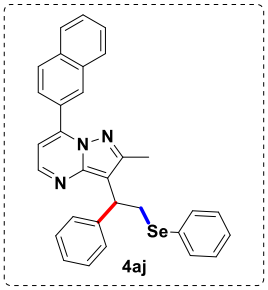


4ah

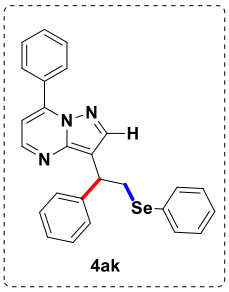
7-(4-Fluorophenyl)-2-methyl-3-(1-phenyl-2-(phenylselanyl)ethyl)pyrazolo[1,5-*a*]pyrimidine(4ah): Yellow gummy mass; 91% (88.6 mg); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.33 (d, *J* = 4.3 Hz, 1H), 7.97 (dd, *J* = 8.7, 5.5 Hz, 2H), 7.42 (d, *J* = 7.8 Hz, 2H), 7.36 (dd, *J* = 6.6, 3.0 Hz, 2H), 7.21 (t, *J* = 7.6 Hz, 2H), 7.18 – 7.08 (m, 6H), 6.62 (d, *J* = 4.4 Hz, 1H), 4.41 (dd, *J* = 10.5, 5.5 Hz, 1H), 4.29 (t, *J* = 11.1 Hz, 1H), 3.68 (dd, *J* = 11.8, 5.6 Hz, 1H), 2.31 (s, 3H). **^{13}C {^{1}H} NMR** (126 MHz, $CDCl_3$) δ 165.1, 163.1, 153.5, 147.7, 147.6, 144.7, 144.5, 133.0, 131.5, 131.4, 130.4, 128.8, 128.6, 127.7, 127.4, 127.3 126.7, 126.6, 115.9, 115.8, 109.2, 106.3, 43.4, 33.0, 13.3; **HRMS** (ESI, *m/z*): Calculated for $C_{27}H_{23}FN_3Se$ $[M+H]^+$: 488.1037, found 488.1037.



7-(4-Bromophenyl)-2-methyl-3-(1-phenyl-2-(phenylselanyl)ethyl)pyrazolo[1,5-*a*]pyrimidine(4ai): Yellow oil; 87% (95.2 mg); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.38 (d, *J* = 4.4 Hz, 1H), 7.91 – 7.84 (m, 2H), 7.68 – 7.61 (m, 2H), 7.46 – 7.41 (m, 2H), 7.41 – 7.36 (m, 2H), 7.25 (s, 1H), 7.24 – 7.21 (m, 1H), 7.18 – 7.10 (m, 4H), 6.69 (d, *J* = 4.3 Hz, 1H), 4.43 (dd, *J* = 10.5, 5.6 Hz, 1H), 4.36 – 4.26 (m, 1H), 3.70 (dd, *J* = 11.9, 5.5 Hz, 1H), 2.33 (s, 3H); **^{13}C {^{1}H} NMR** (126 MHz, $CDCl_3$) δ 153.6, 147.7, 147.6, 144.8, 144.5, 133.1, 132.0, 130.9, 130.4, 130.2, 128.8, 128.6, 127.8, 126.8, 126.7, 125.5, 109.4, 106.3, 43.5, 33.0, 13.4; **HRMS** (ESI, *m/z*): Calculated for $C_{27}H_{23}BrN_3Se$ $[M+H]^+$: 548.0234, found 548.0231.

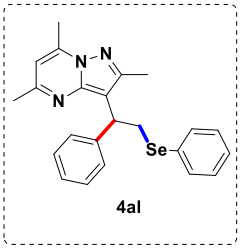


2-Methyl-7-(naphthalen-2-yl)-3-(1-phenyl-2-(phenylselanyl)ethyl)pyrazolo[1,5-*a*]pyrimidine(4aj): Orange oil; 71% (73.7 mg); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.49 (s, 1H), 8.37 (d, *J* = 4.1 Hz, 1H), 7.98 (d, *J* = 8.5 Hz, 1H), 7.89 (t, *J* = 9.5 Hz, 2H), 7.83 (d, *J* = 9.2 Hz, 1H), 7.48 (dd, *J* = 15.2, 7.7 Hz, 4H), 7.43 – 7.37 (m, 2H), 7.24 (d, *J* = 7.8 Hz, 2H), 7.18 – 7.09 (m, 4H), 6.75 (d, *J* = 4.3 Hz, 1H), 4.46 (dd, *J* = 10.5, 5.6 Hz, 1H), 4.34 (t, *J* = 11.1 Hz, 1H), 3.73 (dd, *J* = 11.9, 5.6 Hz, 1H), 2.35 (s, 3H); **^{13}C {^{1}H} NMR** (126 MHz, $CDCl_3$) δ 153.4, 147.7, 145.9, 144.5, 134.4, 133.0, 132.9, 130.4, 129.8, 129.0, 128.8, 128.7, 128.6, 128.2, 127.8, 127.7, 127.6, 126.7, 126.6, 126.5, 125.7, 109.2, 106.8, 43.4, 33.0, 13.4; **HRMS** (ESI, *m/z*): Calculated for $C_{31}H_{26}N_3Se$ $[M+H]^+$: 520.1289, found 520.1288.



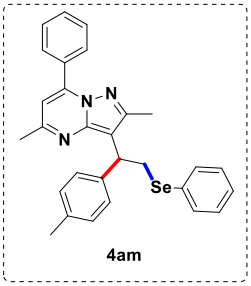
4ak

7-phenyl-3-(1-phenyl-2-(phenylselanyl)ethyl)pyrazolo[1,5-*a*]pyrimidine(4ak): Yellow oil; 83% (75.5 mg); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.38 (d, *J* = 4.3 Hz, 1H), 8.02 (s, 1H), 7.92 (dd, *J* = 6.7, 3.1 Hz, 2H), 7.50 – 7.45 (m, 3H), 7.40 (dd, *J* = 7.2, 2.4 Hz, 4H), 7.24 (d, *J* = 7.9 Hz, 2H), 7.14 (ddd, *J* = 16.2, 5.9, 1.9 Hz, 4H), 6.73 (d, *J* = 4.3 Hz, 1H), 4.73 – 4.62 (m, 1H), 3.97 (dd, *J* = 12.0, 9.1 Hz, 1H), 3.61 (dd, *J* = 12.1, 6.9 Hz, 1H); **^{13}C {^{1}H} NMR** (126 MHz, $CDCl_3$) δ 148.1, 146.8, 146.5, 144.0, 143.5, 132.8, 131.0, 130.9, 130.6, 129.2, 128.9, 128.7, 128.6, 127.7, 126.7, 112.5, 107.3, 42.6, 34.0; **HRMS** (ESI, *m/z*): Calculated for $C_{26}H_{22}N_3Se$ $[M+H]^+$: 456.0975, found 456.0989.



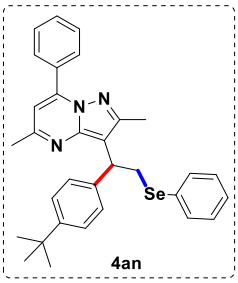
4al

2,5,7-trimethyl-3-(1-phenyl-2-(phenylselanyl)ethyl)pyrazolo[1,5-*a*]pyrimidine(4al):Brown oil; 79% (66.5 mg); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.45 – 7.39 (m, 4H), 7.26 – 7.22 (m, 2H), 7.17 (q, *J* = 3.6 Hz, 4H), 6.42 (s, 1H), 4.42 – 4.31 (m, 2H), 3.70 (dd, *J* = 11.3, 5.2 Hz, 1H), 2.64 (s, 3H), 2.54 (s, 3H), 2.33 (s, 3H); **^{13}C {^{1}H} NMR** (126 MHz, $CDCl_3$) δ 157.3, 152.8, 146.5, 144.7, 144.4, 133.0, 130.6, 128.8, 128.6, 127.8, 126.8, 126.6, 108.0, 107.7, 43.2, 33.4, 24.9, 17.2, 13.2; **HRMS** (ESI, *m/z*): Calculated for $C_{23}H_{24}N_3Se$ $[M+H]^+$: 422.1131, found 422.1135.



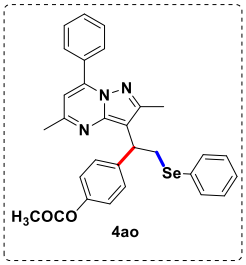
4am

2,5-Dimethyl-7-phenyl-3-(2-(phenylselanyl)-1-(p-tolyl)ethyl)pyrazolo[1,5-*a*]pyrimidine(4am): Yellow jelly; 85% (84.5 mg); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.95 – 7.89 (m, 2H), 7.48 – 7.44 (m, 3H), 7.41 – 7.36 (m, 2H), 7.34 (d, *J* = 8.1 Hz, 2H), 7.14 – 7.08 (m, 3H), 7.04 (d, *J* = 8.1 Hz, 2H), 6.52 (s, 1H), 4.37 (dd, *J* = 10.2, 5.3 Hz, 1H), 4.34 – 4.27 (m, 1H), 3.69 (dd, *J* = 11.4, 5.5 Hz, 1H), 2.54 (s, 3H), 2.28 (s, 3H), 2.24 (s, 3H); **^{13}C {^{1}H} NMR** (126 MHz, $CDCl_3$) δ 157.2, 153.1, 147.4, 145.1, 141.9, 136.0, 133.0, 131.6, 130.7, 129.3, 129.2, 129.1, 128.7, 128.6, 127.7, 126.6, 108.1, 107.4, 43.0, 33.2, 25.0, 21.1, 13.4; **HRMS** (ESI, *m/z*): Calculated for $C_{29}H_{28}N_3Se$ $[M+H]^+$: 498.1445, found 498.1452.



4an

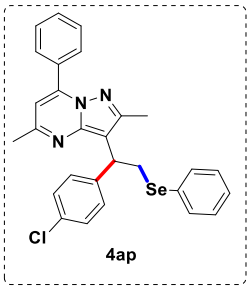
3-(1-(4-(tert-butyl)phenyl)-2-(phenylselanyl)ethyl)-2,5-dimethyl-7-phenylpyrazolo[1,5-*a*]pyrimidine(4an): Orange oil; 82% (88.4 mg**); ^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.00 (dd, *J* = 6.6, 3.1 Hz, 2H), 7.57 – 7.52 (m, 3H), 7.49 – 7.42 (m, 4H), 7.33 (d, *J* = 8.4 Hz, 2H), 7.22 – 7.15 (m, 3H), 6.61 (s, 1H), 4.44 (d, *J* = 7.9 Hz, 2H), 3.77 – 3.67 (m, 1H), 2.63 (s, 3H), 2.38 (s, 3H), 1.32 (s, 9H); **^{13}C {^{1}H} NMR** (126 MHz, $CDCl_3$) δ 157.1, 153.2, 149.2, 147.4, 145.1, 141.9, 133.1, 131.6, 130.7, 130.6, 129.3, 128.7, 128.6, 127.5, 126.6, 125.4, 108.1, 107.4, 43.1, 34.5, 33.3, 31.5, 25.0, 13.6; **HRMS** (ESI, *m/z*): Calculated for $C_{32}H_{34}N_3Se$ $[M+H]^+$: 540.1915, found 540.1915.



4ao

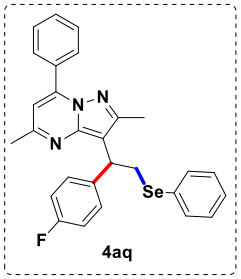
4-(1-(2,5-Dimethyl-7-phenylpyrazolo[1,5-*a*]pyrimidin-3-yl)-2-(phenylselanyl)ethyl)phenyl acetate(4ao): Yellow jelly; 78% (84.4 mg); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.89 – 7.83 (m, 2H), 7.42 – 7.37 (m, 5H), 7.31 (dd, *J* = 6.6, 3.1 Hz, 2H), 7.07 – 7.02 (m, 3H), 6.88 (d, *J* = 8.7 Hz, 2H), 6.48 (s, 1H), 4.33 – 4.23 (m, 2H), 3.59 (dd, *J* = 10.9, 4.5 Hz, 1H), 2.47 (s, 3H), 2.22 (s, 3H), 2.14 (s, 3H); **^{13}C {^{1}H} NMR** (126 MHz, $CDCl_3$) δ 168.5, 156.2, 152.0, 148.1, 146.3, 144.1, 141.3, 132.0, 130.4, 129.6, 129.3, 128.1,

127.7, 127.6, 127.5, 125.6, 120.3, 106.5, 106.4, 41.8, 32.1, 23.9, 20.1, 12.2; **HRMS** (ESI, *m/z*): Calculated for $C_{30}H_{27}N_3O_2SeNa$ $[M+Na]^+$: 564.1163, found 564.1162.



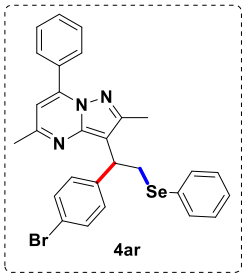
4ap

3-(1-(4-Chlorophenyl)-2-(phenylselanyl)ethyl)-2,5-dimethyl-7-phenylpyrazolo[1,5-*a*]pyrimidine(4ap):Yellow oil; 71% (73.4 mg); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.97 (dd, *J* = 6.7, 3.1 Hz, 2H), 7.54 – 7.51 (m, 3H), 7.43 – 7.39 (m, 4H), 7.23 (d, *J* = 8.5 Hz, 2H), 7.19 – 7.15 (m, 3H), 6.61 (s, 1H), 4.42 – 4.36 (m, 1H), 4.31 – 4.25 (m, 1H), 3.71 (dd, *J* = 11.9, 6.0 Hz, 1H), 2.61 (s, 3H), 2.31 (s, 3H); **^{13}C {^{1}H} NMR** (126 MHz, $CDCl_3$) δ 157.5, 153.1, 147.2, 145.5, 143.2, 133.2, 132.3, 131.5, 130.9, 130.4, 129.3, 129.2, 128.8, 128.7, 128.6, 126.9, 107.6, 107.5, 42.9, 33.0, 25.0, 13.4; **HRMS** (ESI, *m/z*): Calculated for $C_{28}H_{25}ClN_3Se$ $[M+H]^+$: 518.0896, found 518.0904.



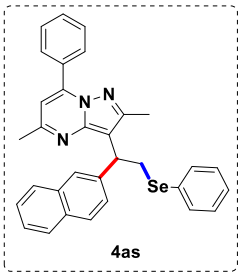
4aq

3-(1-(4-Fluorophenyl)-2-(phenylselanyl)ethyl)-2,5-dimethyl-7-phenylpyrazolo[1,5-*a*]pyrimidine(4aq):Yellow oil; 89% (89.2 mg); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.03 – 7.95 (m, 2H), 7.57 – 7.51 (m, 3H), 7.50 – 7.41 (m, 4H), 7.23 – 7.14 (m, 3H), 7.02 – 6.93 (m, 2H), 6.62 (s, 1H), 4.43 (dd, *J* = 9.9, 6.0 Hz, 1H), 4.31 (dd, *J* = 12.0, 10.0 Hz, 1H), 3.73 (dd, *J* = 11.9, 6.0 Hz, 1H), 2.62 (s, 3H), 2.34 (s, 3H); **^{13}C {^{1}H} NMR** (126 MHz, $CDCl_3$) δ 162.3, 160.4, 157.2, 152.8, 147.1, 145.1, 140.3, 140.3, 132.9, 131.3, 130.5, 130.2, 129.1, 129.0, 128.9, 128.5, 128.4, 126.5, 115.1, 114.9, 107.6, 107.3, 42.5, 33.0, 24.7, 13.1; **HRMS** (ESI, *m/z*): Calculated for $C_{28}H_{25}FN_3Se$ $[M+H]^+$: 502.1194, found 502.1193.



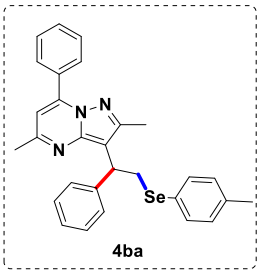
4ar

3-(1-(4-Bromophenyl)-2-(phenylselanyl)ethyl)-2,5-dimethyl-7-phenylpyrazolo[1,5-*a*]pyrimidine(4ar): Brown oil; 68% (76.3 mg); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.98 (dd, *J* = 6.6, 3.1 Hz, 2H), 7.66 – 7.46 (m, 4H), 7.42 (dd, *J* = 6.6, 3.1 Hz, 2H), 7.38 (d, *J* = 1.7 Hz, 3H), 7.20 – 7.15 (m, 3H), 6.62 (s, 1H), 4.39 (dd, *J* = 9.9, 6.0 Hz, 1H), 4.31 – 4.23 (m, 1H), 3.72 (dd, *J* = 12.0, 6.0 Hz, 1H), 2.61 (s, 3H), 2.32 (s, 3H); **^{13}C {^{1}H} NMR** (126 MHz, $CDCl_3$) δ 157.5, 153.1, 147.3, 145.4, 143.7, 133.2, 131.6, 131.5, 130.8, 130.3, 129.7, 129.3, 128.8, 128.7, 126.8, 120.4, 107.6, 107.5, 42.9, 32.9, 25.0, 13.4; **HRMS** (ESI, *m/z*): Calculated for $C_{28}H_{25}BrN_3Se$ $[M+H]^+$: 562.0391, found 562.0380.

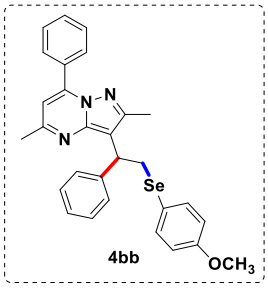


4as

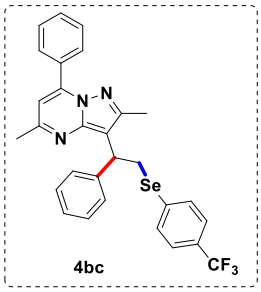
2,5-Dimethyl-3-(1-(naphthalen-2-yl)-2-(phenylselanyl)ethyl)-7-phenylpyrazolo[1,5-*a*]pyrimidine(4as):Brown jelly; 81% (86.4 mg); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.00 (dd, *J* = 6.8, 3.0 Hz, 2H), 7.86 (s, 1H), 7.82 – 7.74 (m, 3H), 7.70 (d, *J* = 8.4 Hz, 1H), 7.57 – 7.50 (m, 3H), 7.50 – 7.39 (m, 4H), 7.23 – 7.14 (m, 3H), 6.63 (s, 1H), 4.70 – 4.55 (m, 1H), 4.44 (t, *J* = 11.1 Hz, 1H), 3.86 (dd, *J* = 12.0, 5.9 Hz, 1H), 2.65 (s, 3H), 2.36 (s, 3H); **^{13}C {^{1}H} NMR** (126 MHz, $CDCl_3$) δ 157.4, 153.4, 147.4, 145.4, 142.1, 133.6, 133.1, 132.4, 131.6, 130.8, 130.7, 129.3, 128.8, 128.7, 128.3, 127.9, 127.7, 126.8, 126.7, 126.0, 125.9, 125.5, 107.9, 107.6, 43.5, 33.0, 25.0, 13.5; **HRMS** (ESI, *m/z*): Calculated for $C_{32}H_{28}N_3Se$ $[M+H]^+$: 534.1445, found 534.1445.



2,5-Dimethyl-7-phenyl-3-(1-phenyl-2-(p-tolylselanyl)ethyl)pyrazolo[1,5-a]pyrimidine(4ba): Yellow jelly; 80% (79.5 mg); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.92 (dd, *J* = 6.8, 3.0 Hz, 2H), 7.50 – 7.39 (m, 5H), 7.28 (s, 2H), 7.21 (t, *J* = 7.6 Hz, 2H), 7.12 (t, *J* = 7.3 Hz, 1H), 6.92 (d, *J* = 8.1 Hz, 2H), 6.53 (s, 1H), 4.38 (dd, *J* = 10.5, 5.4 Hz, 1H), 4.29 (t, *J* = 11.1 Hz, 1H), 3.62 (dd, *J* = 11.7, 5.5 Hz, 1H), 2.54 (s, 3H), 2.28 (s, 3H), 2.22 (s, 3H); **^{13}C {^{1}H} NMR** (126 MHz, $CDCl_3$) δ 157.2, 153.2, 147.4, 145.2, 144.9, 136.6, 133.6, 131.6, 130.7, 129.5, 129.3, 128.6, 128.5, 127.8, 126.7, 126.5, 108.0, 107.4, 43.5, 33.4, 25.0, 21.2, 13.4; **HRMS** (ESI, *m/z*): Calculated for $C_{29}H_{28}N_3Se$ $[M+H]^+$: 498.1445, found 498.1444.

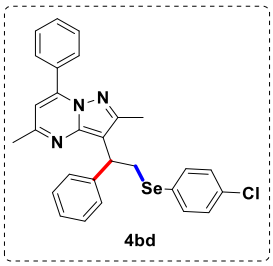


3-(2-((4-Methoxyphenyl)selanyl)-1-phenylethyl)-2,5-dimethyl-7-phenylpyrazolo[1,5-*a*]pyrimidine(4bb): Yellow oil; 87% (89.3 mg); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.99 (dd, *J* = 6.6, 3.0 Hz, 2H), 7.58 – 7.51 (m, 3H), 7.48 (d, *J* = 7.5 Hz, 2H), 7.35 (d, *J* = 8.7 Hz, 2H), 7.30 – 7.25 (m, 2H), 7.18 (t, *J* = 7.4 Hz, 1H), 6.70 (d, *J* = 8.7 Hz, 2H), 6.59 (s, 1H), 4.42 (dd, *J* = 10.7, 5.0 Hz, 1H), 4.34 (t, *J* = 11.1 Hz, 1H), 3.75 (s, 3H), 3.61 (dd, *J* = 11.7, 5.1 Hz, 1H), 2.60 (s, 3H), 2.37 (s, 3H); **^{13}C {^{1}H} NMR** (126 MHz, $CDCl_3$) δ 159.1, 157.2, 153.2, 147.9, 145.1, 145.0, 135.8, 131.6, 130.7, 129.3, 128.6, 128.5, 127.8, 126.5, 120.3, 114.3, 107.9, 107.4, 55.3, 43.7, 33.9, 25.0, 13.5; **HRMS** (ESI, *m/z*): Calculated for $C_{29}H_{28}N_3OSe$ $[M+H]^+$: 514.1394, found 514.1395.



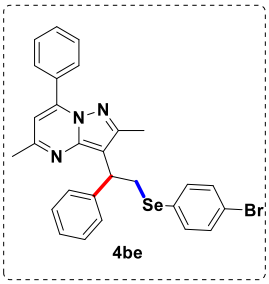
4bc

2,5-Dimethyl-7-phenyl-3-(1-phenyl-2-((4-(trifluoromethyl)phenyl)selanyl)ethyl)pyrazolo[1,5-*a*]pyrimidine(4bc): Yellow gummy mass; 88% (97.0 mg); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.98 (dt, *J* = 5.2, 3.0 Hz, 2H), 7.56 – 7.50 (m, 5H), 7.48 (d, *J* = 8.4 Hz, 2H), 7.38 (d, *J* = 8.4 Hz, 2H), 7.30 (t, *J* = 7.6 Hz, 2H), 7.22 (d, *J* = 7.3 Hz, 1H), 6.60 (s, 1H), 4.58 – 4.35 (m, 2H), 3.80 (dd, *J* = 11.3, 5.0 Hz, 1H), 2.59 (s, 3H), 2.36 (s, 3H); **^{13}C {^{1}H} NMR** (126 MHz, $CDCl_3$) δ 157.4, 153.2, 147.4, 145.3, 144.5, 136.4, 132.4, 131.4, 130.9, 129.3, 128.7, 128.6, 128.4, 127.9, 126.8, 125.3 (q, *J* = 3.9 Hz), 107.7, 107.5, 43.8, 33.1, 25.0, 13.5; **HRMS** (ESI, *m/z*): Calculated for $C_{29}H_{25}F_3N_3Se$ $[M+H]^+$: 552.1162, found 552.1165.



4bd

3-(2-((4-Chlorophenyl)selanyl)-1-phenylethyl)-2,5-dimethyl-7-phenylpyrazolo[1,5-a]pyrimidine(4bd): Brown oil; 84% (86.9 mg); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.02 (dd, *J* = 6.5, 3.3 Hz, 2H), 7.61 – 7.47 (m, 5H), 7.36 – 7.27 (m, 4H), 7.25 – 7.18 (m, 1H), 7.10 (dd, *J* = 8.5, 2.1 Hz, 2H), 6.61 (s, 1H), 4.44 (m, 2H), 3.70 (m, 1H), 2.60 (s, 3H), 2.39 (s, 3H); **^{13}C {^{1}H} NMR** (126 MHz, $CDCl_3$) δ 157.3, 153.1, 147.4, 145.1, 144.7, 134.8, 132.9, 131.5, 130.8, 129.3, 128.6, 128.5, 127.8, 126.6, 107.6, 107.4, 44.0, 33.9, 24.9, 13.4; **HRMS** (ESI, *m/z*): Calculated for $C_{28}H_{25}ClN_3Se$ $[M+H]^+$: 518.0896, found 518.0897.



4be

3-(2-((4-bromophenyl)selanyl)-1-phenylethyl)-2,5-dimethyl-7-phenylpyrazolo[1,5-*a*]pyrimidine(4be): Yellow oil; 82% (92.0 mg); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.04 – 7.97 (m, 2H), 7.57 – 7.48 (m, 5H), 7.29 (t, *J* = 7.6 Hz, 2H), 7.22 (s, 5H), 6.61 (s, 1H), 4.45 (dd, *J* = 10.7, 4.9 Hz, 1H), 4.38 (t, *J* = 11.2 Hz, 1H), 3.67 (dd, *J* = 11.6, 4.9 Hz, 1H), 2.59 (s, 3H), 2.38 (s, 3H); **^{13}C {^{1}H} NMR** (126 MHz, $CDCl_3$) δ 157.3, 153.2, 147.3, 145.2, 144.7, 135.1, 131.6, 131.5, 130.8, 129.5, 129.3, 128.7, 128.6, 127.8, 126.7, 121.0, 107.7, 107.4, 44.1, 33.6, 25.0, 13.5; **HRMS** (ESI, *m/z*): Calculated for $C_{28}H_{25}BrN_3Se$ $[M+H]^+$: 562.0391, found 562.0397.

3.4 NMR spectra of compounds

4aa (^{1}H 500MHz/ ^{13}C{^{1}H} 126MHz-CDCl$_3$)

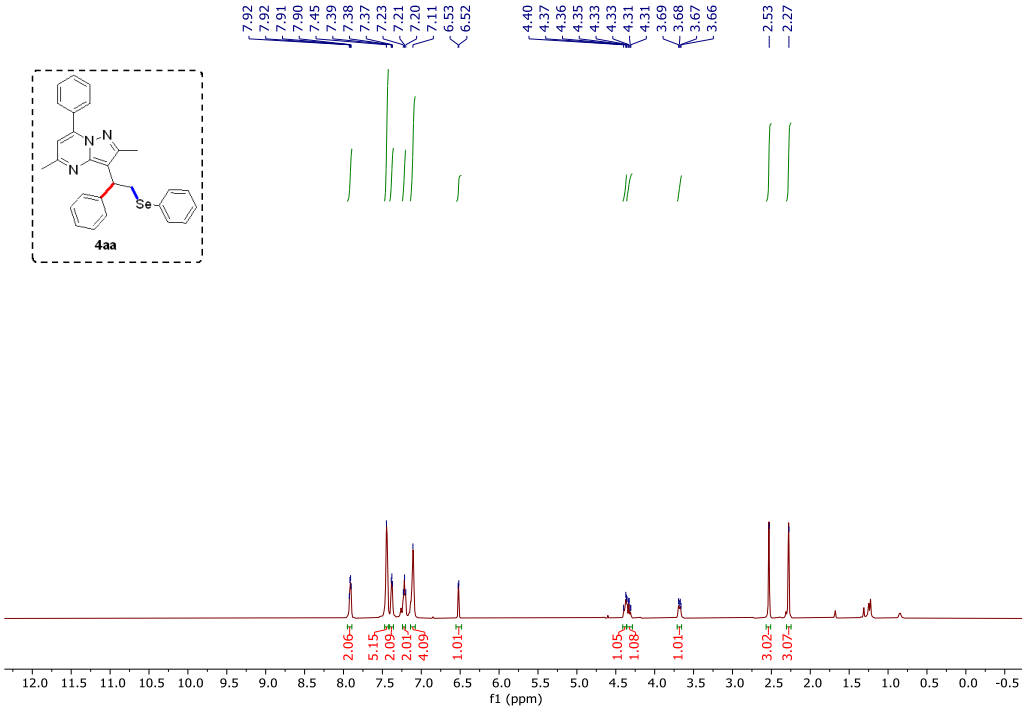


Fig 2: ^{1}H NMR of 4aa

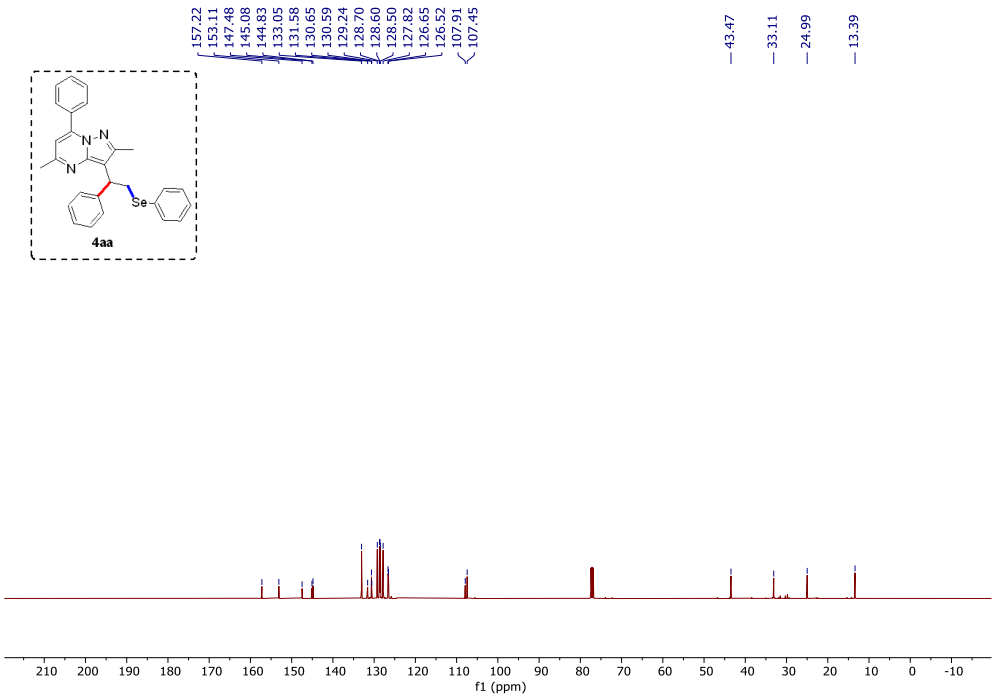


Fig 3: ^{13}C NMR of 4aa

4ab (^{1}H 500MHz/ ^{13}C{^{1}H} 126MHz-CDCl$_3$)

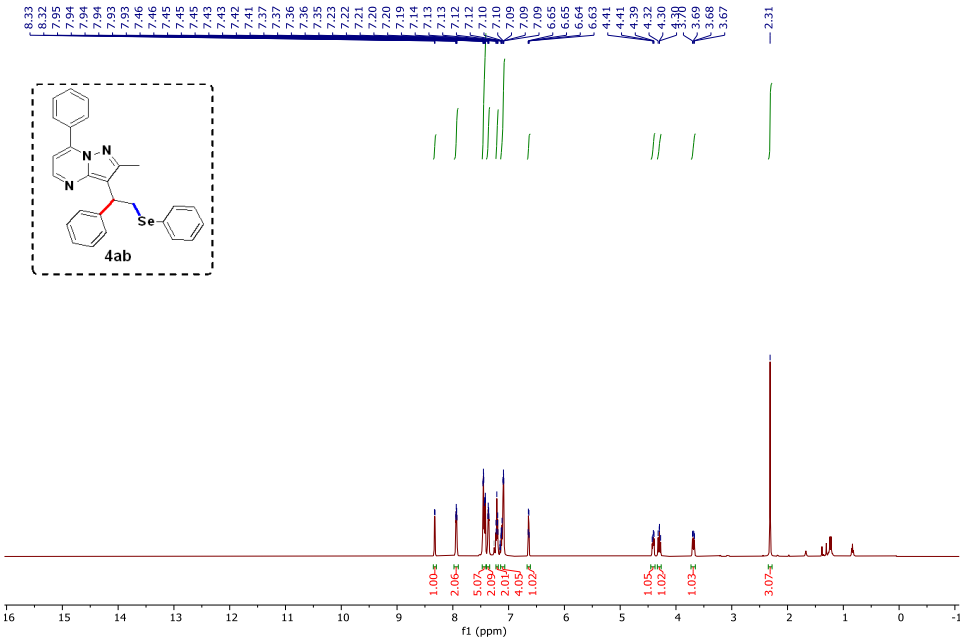


Fig 4: ^{1}H NMR of 4ab

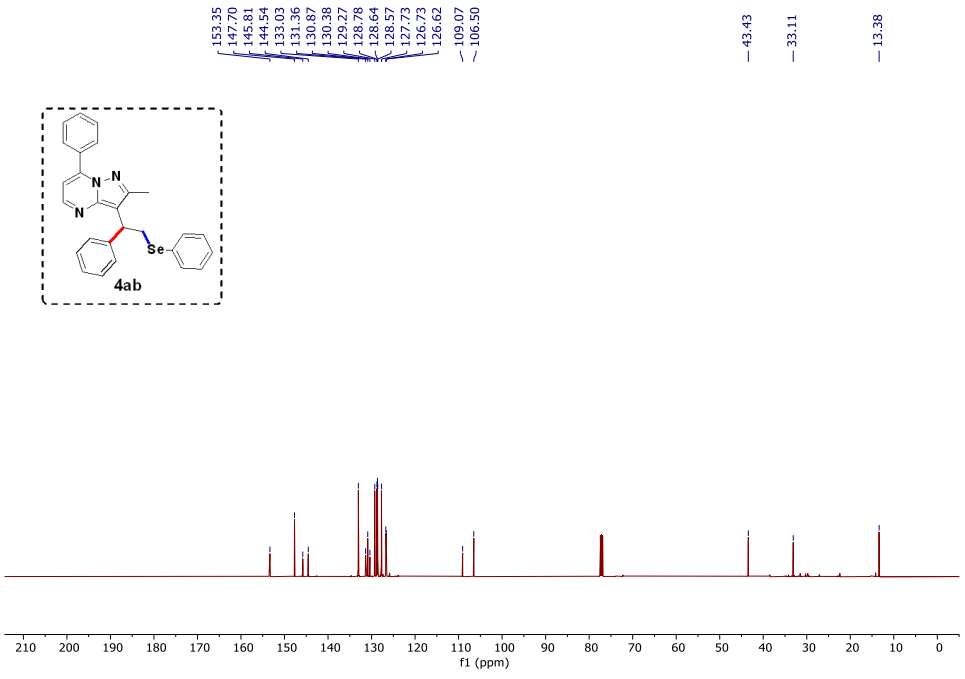


Fig 5: ^{13}C NMR of 4ab

\

4ac (^{1}H 500MHz/ ^{13}C{^{1}H} 126MHz-CDCl$_3$)

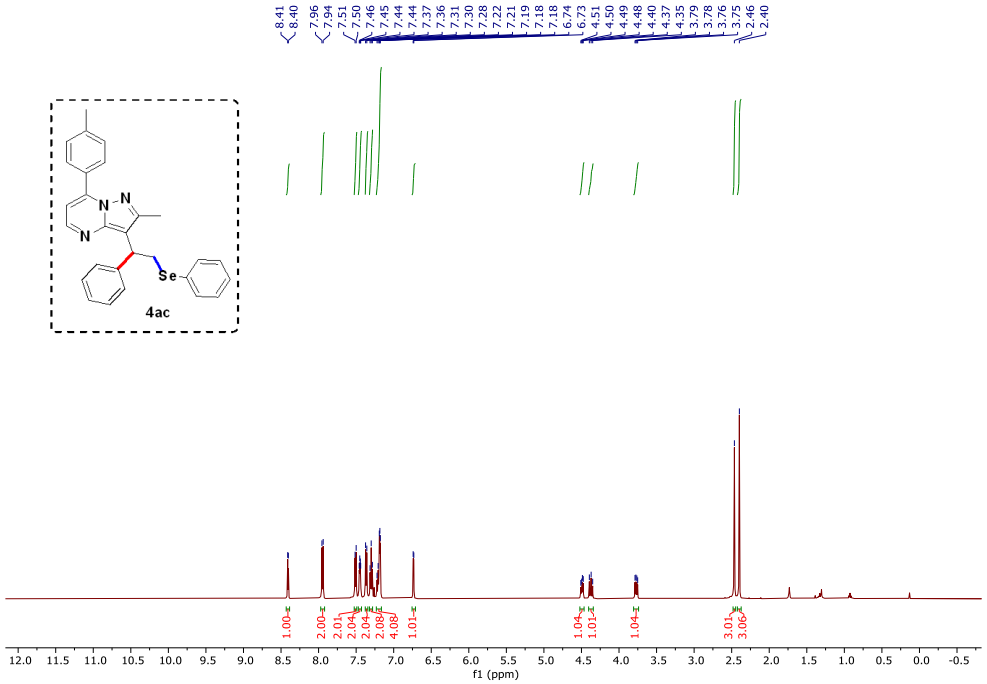


Fig 6: ^{1}H NMR of 4ac

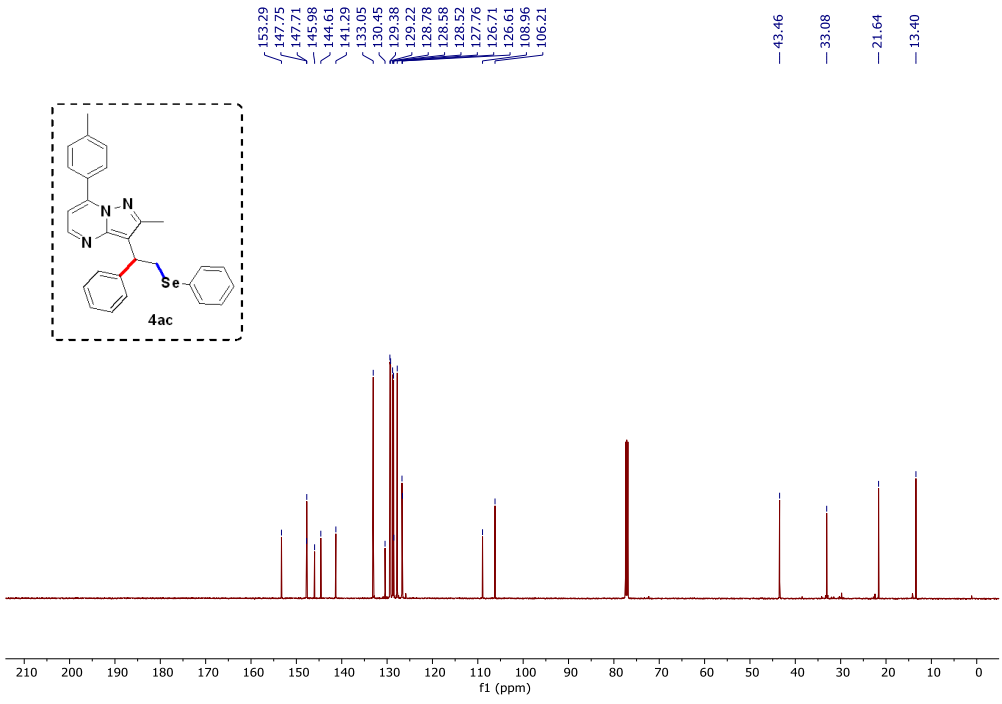


Fig 7: ^{13}C NMR of 4ac

4ad (^{1}H 500MHz/ ^{13}C{^{1}H} 126MHz-CDCl$_3$)

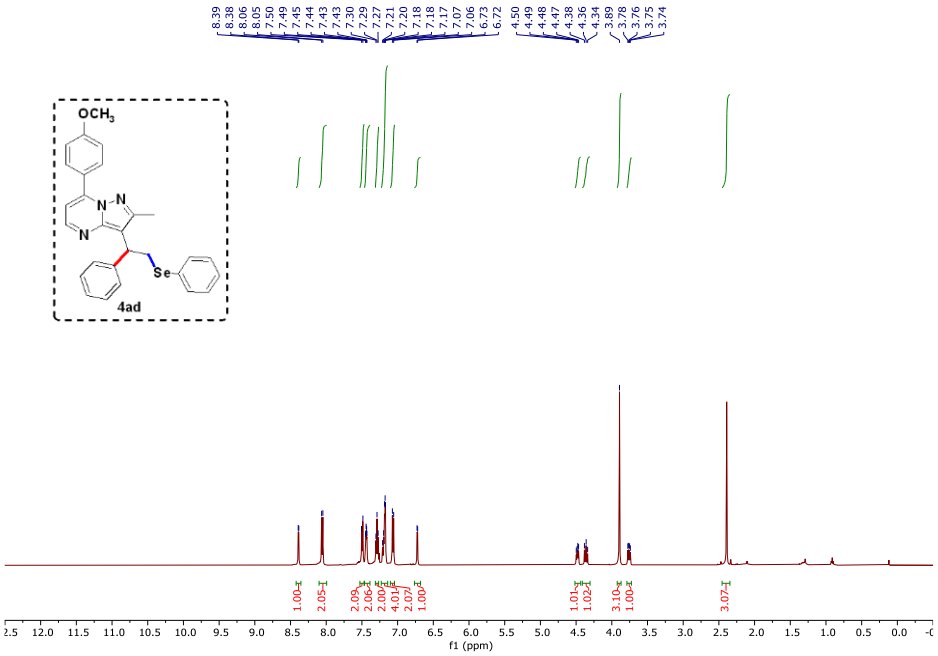


Fig 8: ^{1}H NMR of 4ad

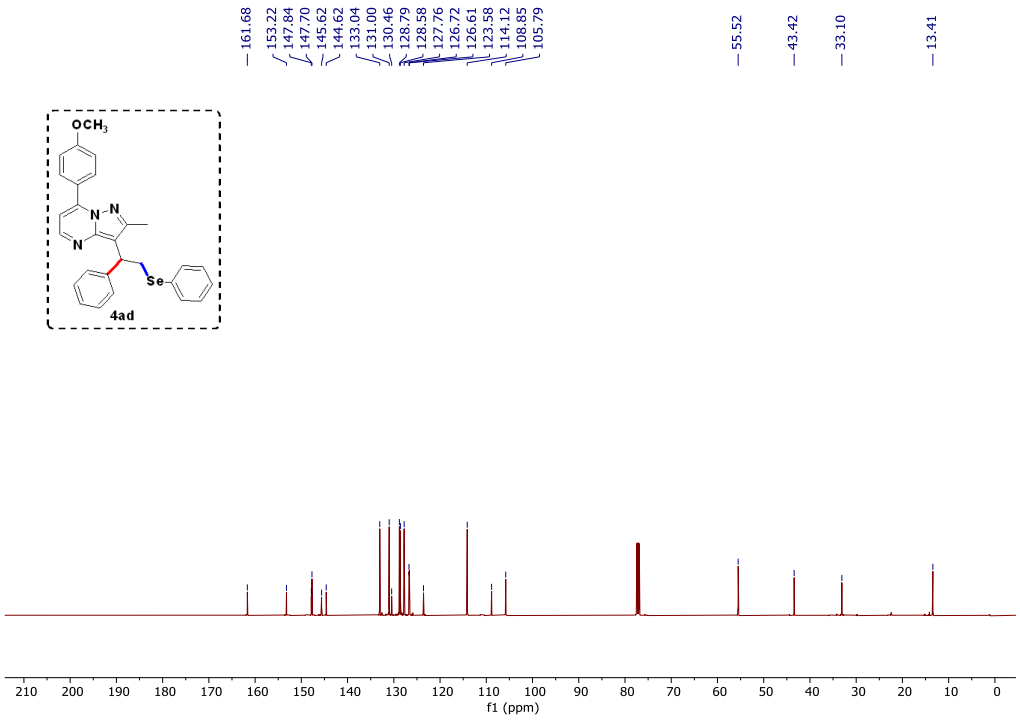


Fig 9: ^{13}C NMR of 4ad

4ae (^{1}H 500MHz/ ^{13}C{^{1}H} 126MHz-CDCl$_3$)

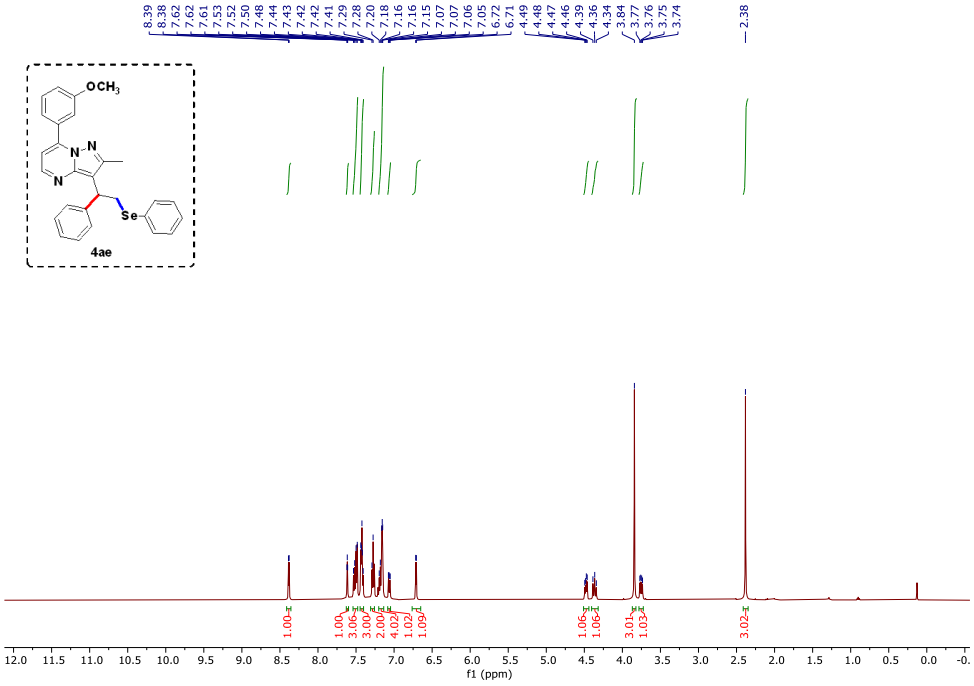


Fig 10: ^{1}H NMR of 4ae

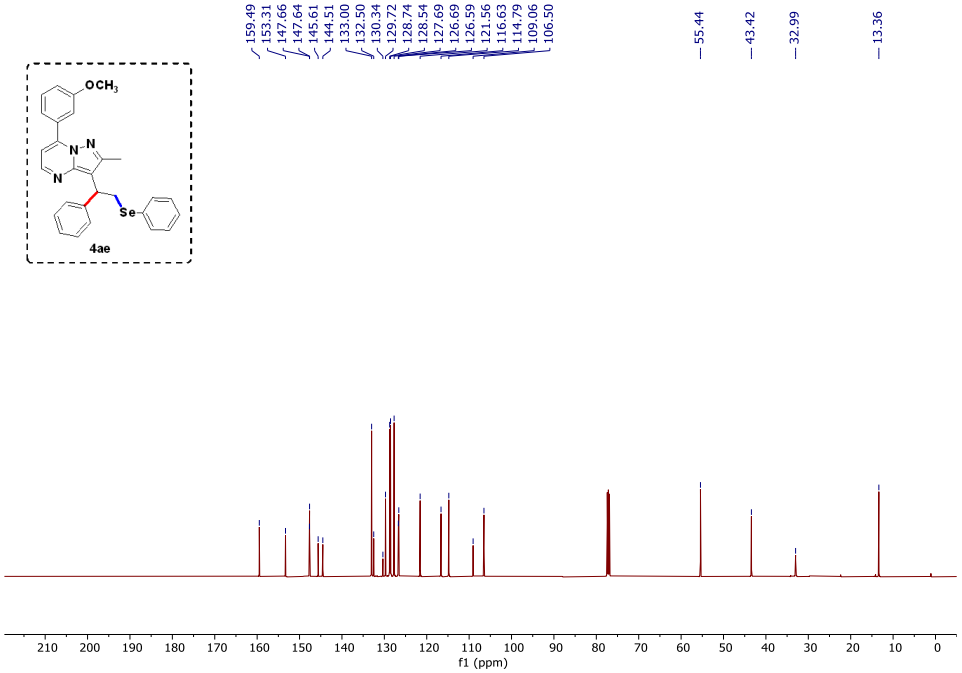


Fig 11: ^{13}C NMR of 4ae

4af (^{1}H 500MHz/ ^{13}C{^{1}H} 126MHz-CDCl$_3$)

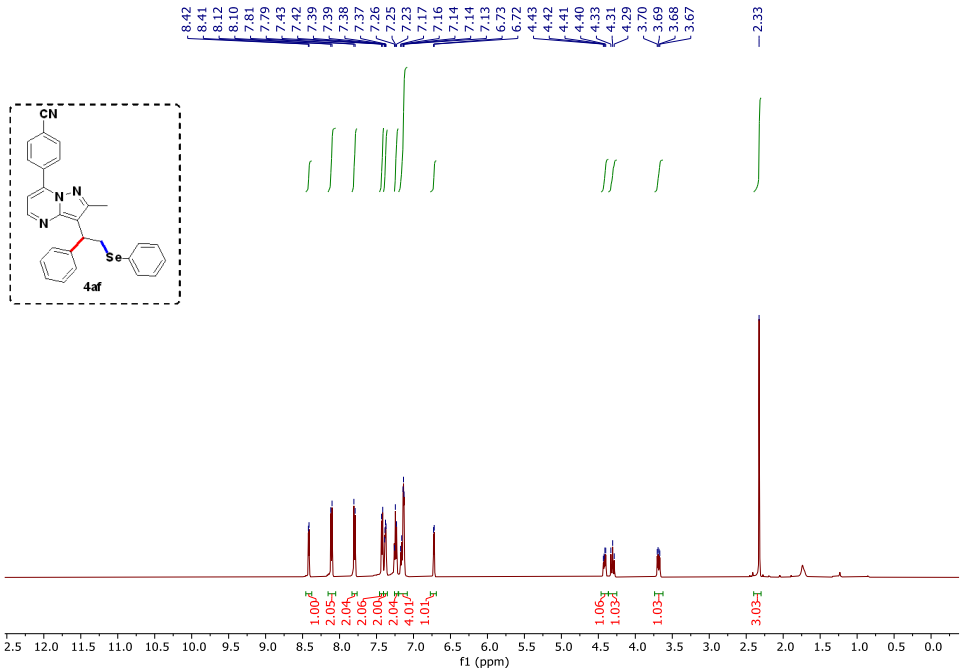


Fig 12: ^{1}H NMR of 4af

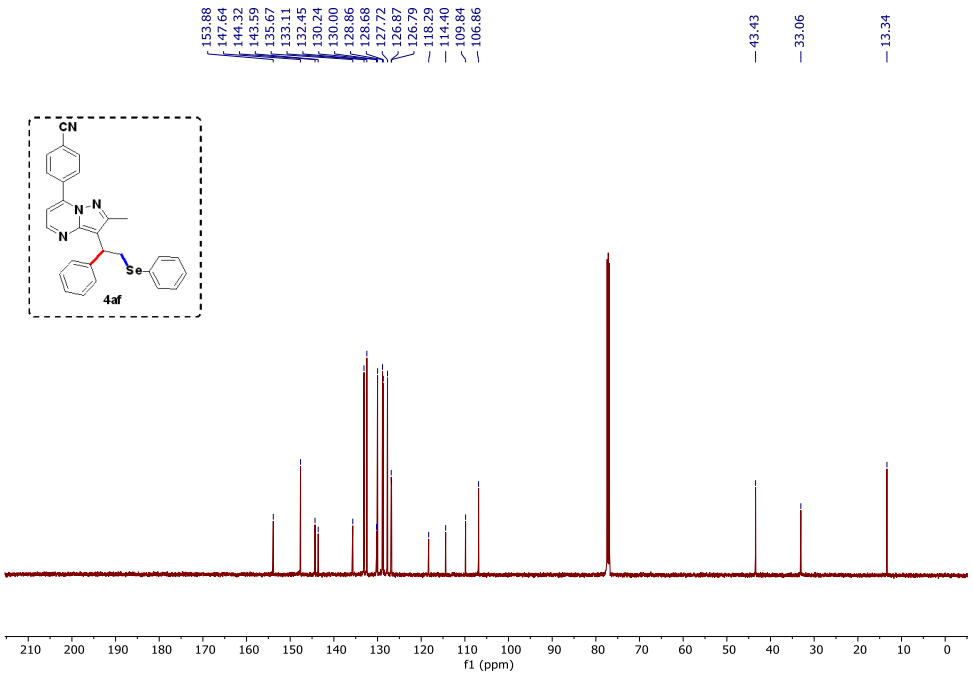


Fig 13: ^{13}C NMR of 4af

4ag (^{1}H 500MHz/ ^{13}C{^{1}H} 126MHz-$CDCl_3$)

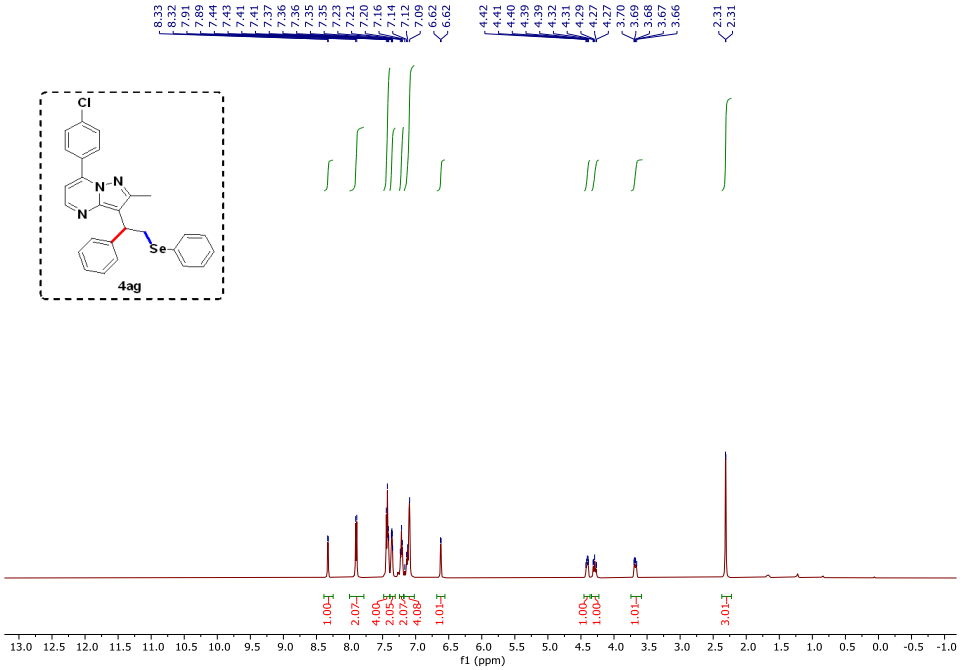


Fig 14: ^{1}H NMR of 4ag

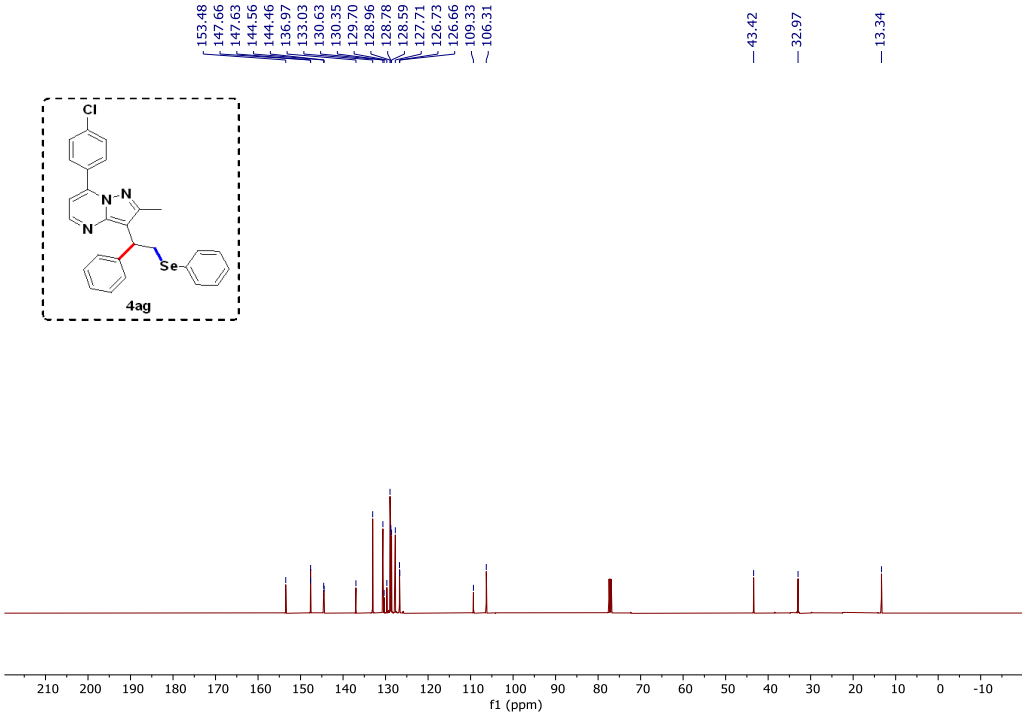


Fig 15: ^{13}C NMR of 4ag

4ah (^{1}H 500MHz/ ^{13}C{^{1}H} 126MHz-CDCl$_3$)

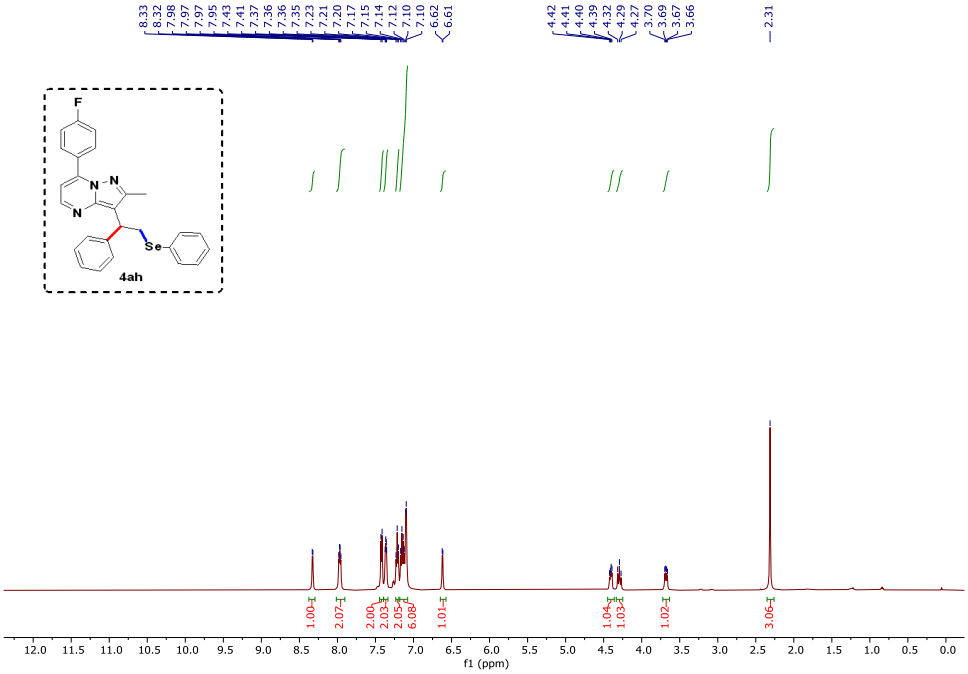


Fig 16: ^{1}H NMR of 4ah

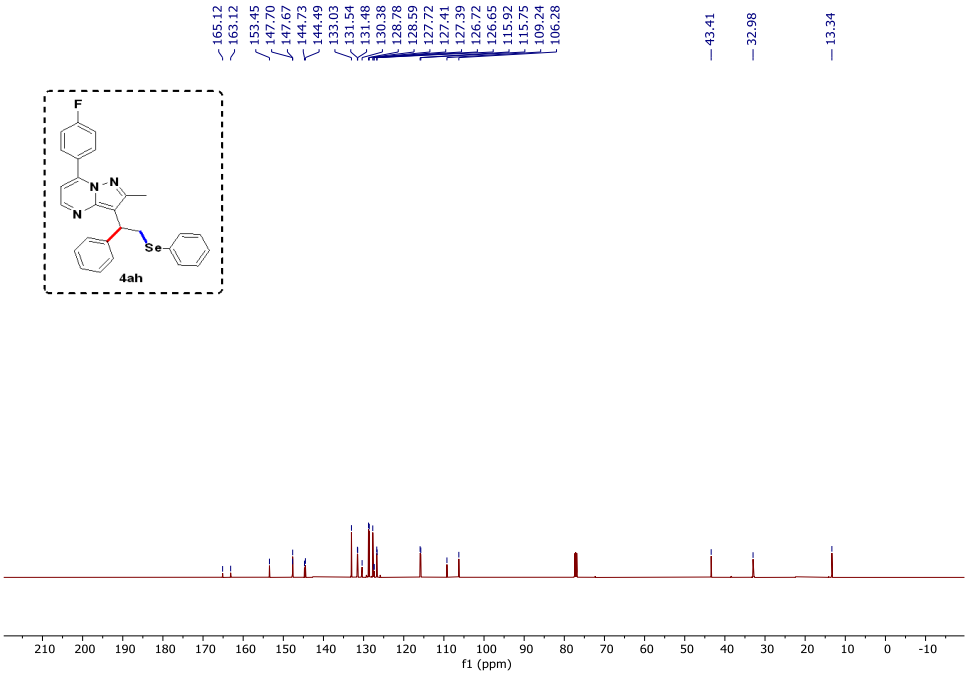


Fig 17: ^{13}C NMR of 4ah

4ai (^{1}H 500MHz/ ^{13}C{^{1}H} 126MHz-CDCl$_3$)

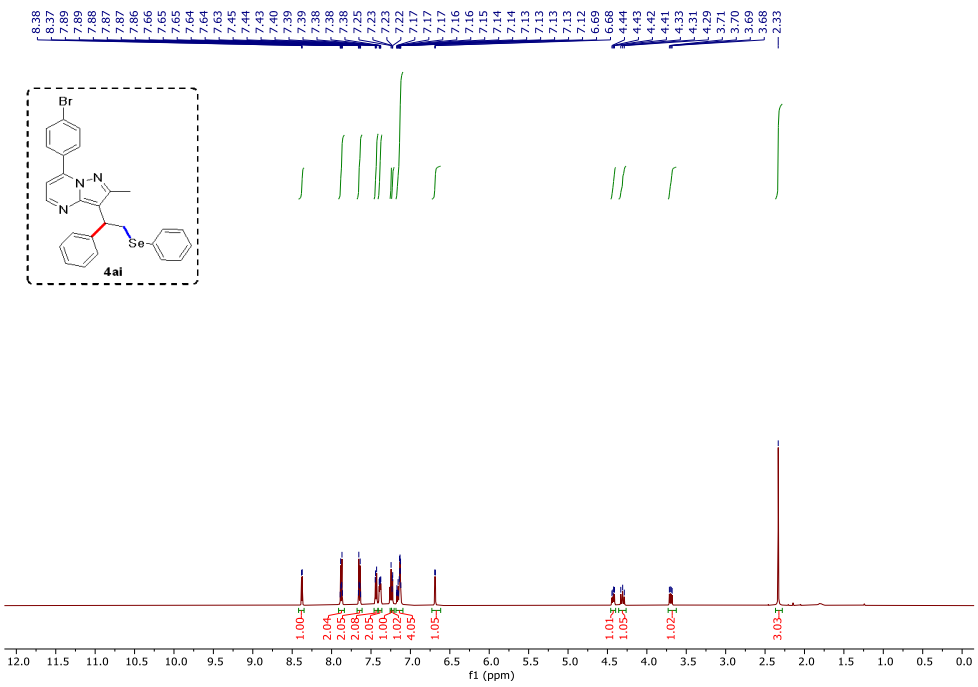


Fig 18: ^{1}H NMR of 4ai

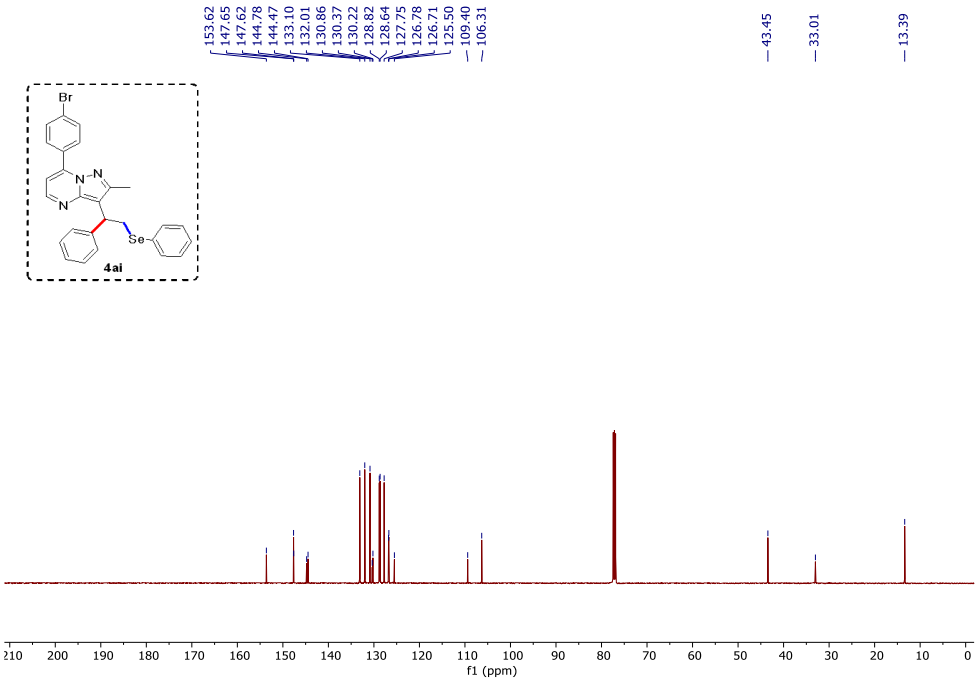


Fig 19: ^{13}C NMR of 4ai

4aj (^{1}H 500MHz/ ^{13}C{^{1}H} 126MHz-$CDCl_3$)

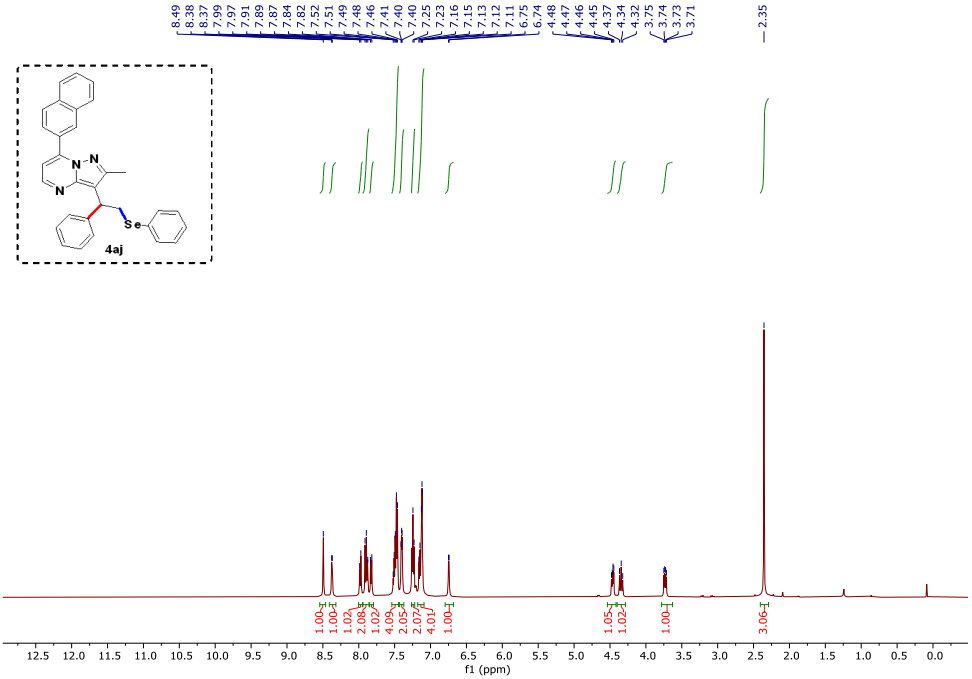


Fig 20: ^{1}H NMR of 4aj

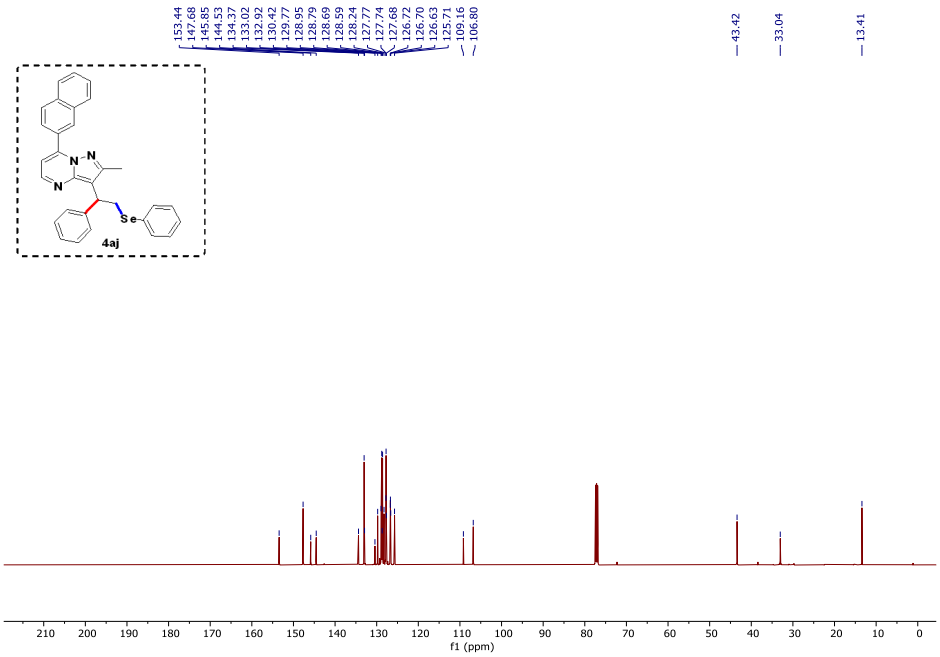


Fig 21: ^{13}C NMR of 4aj

4ak (^{1}H 500MHz/ ^{13}C{^{1}H} 126MHz-CDCl$_3$)

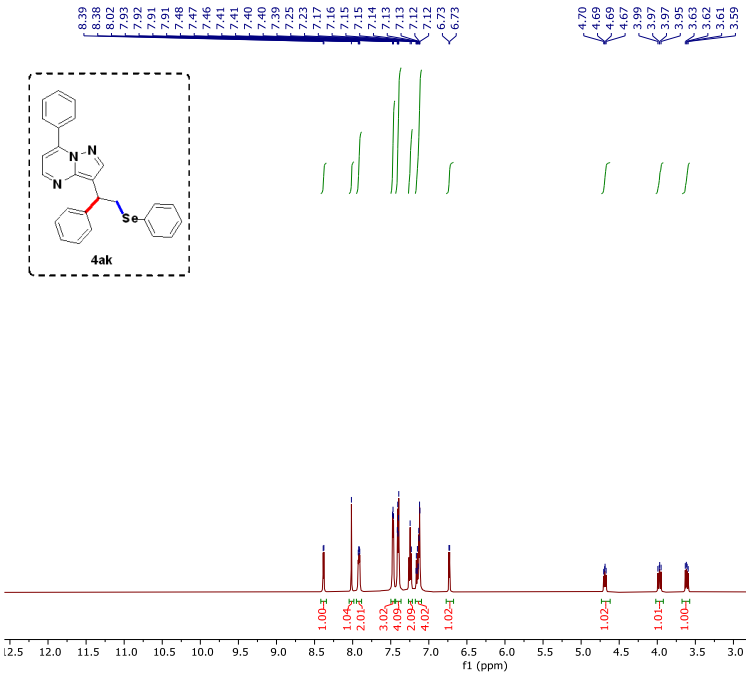


Fig 22: ^{1}H NMR of 4ak

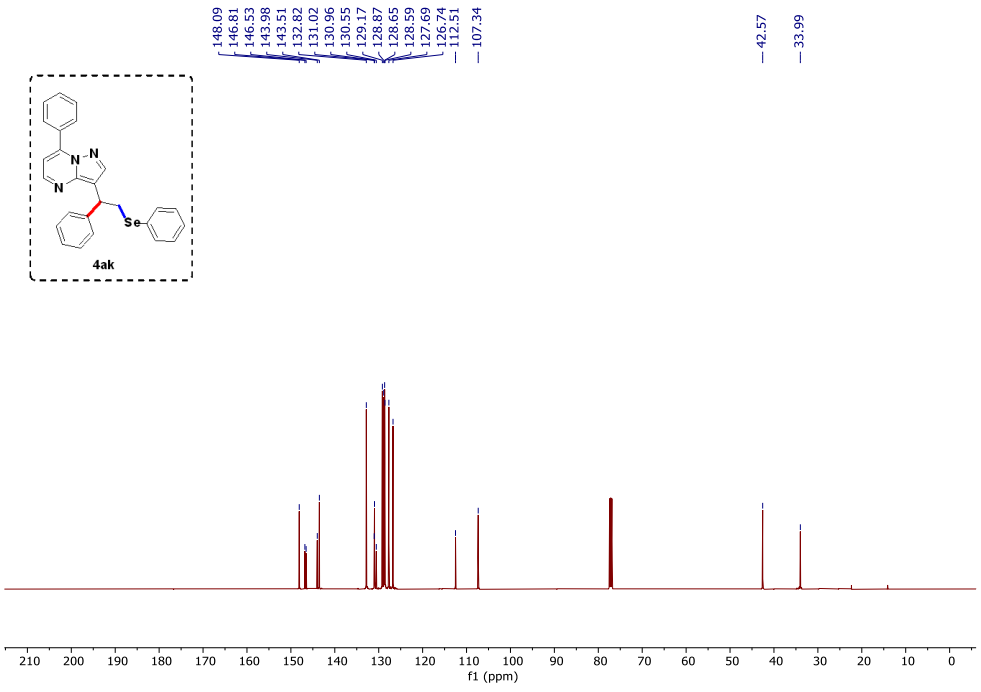


Fig 23: ^{13}C NMR of 4ak

4al (^{1}H 500MHz/ ^{13}C{^{1}H} 126MHz-CDCl$_3$)

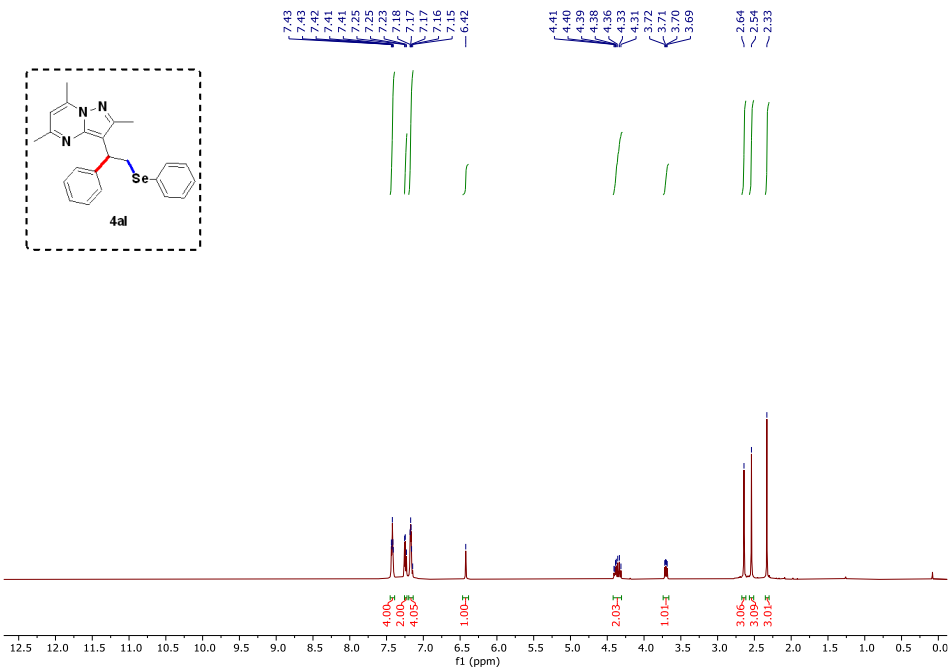


Fig 24: ^{1}H NMR of 4al

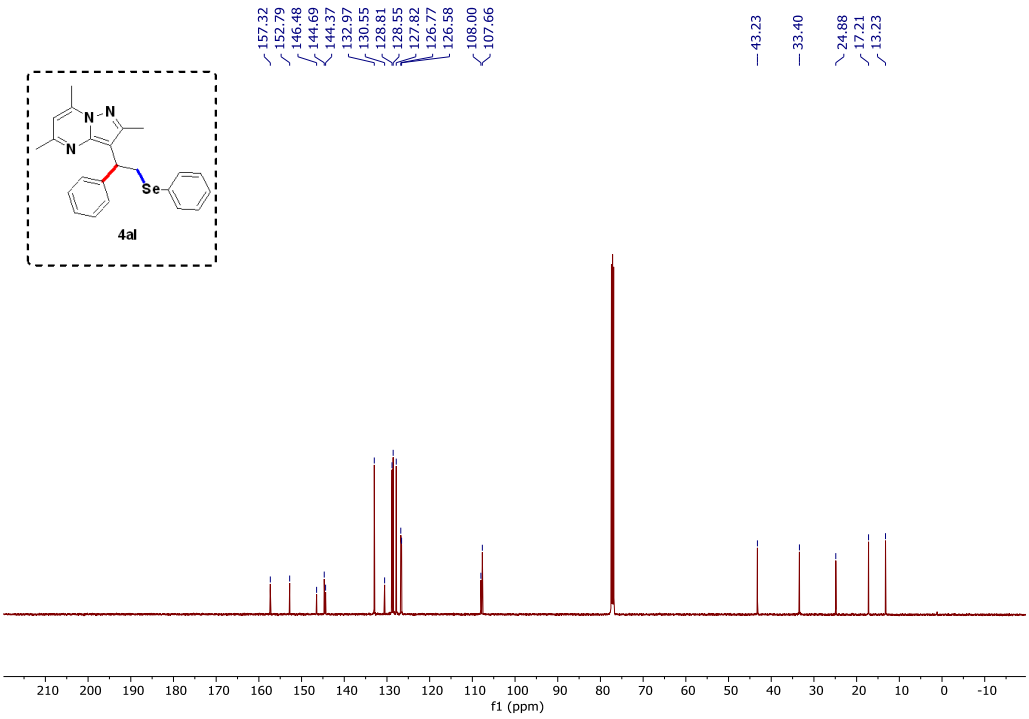


Fig 25: ^{13}C NMR of 4al

4am (^{1}H 500MHz/ ^{13}C{^{1}H} 126MHz-CDCl$_3$)

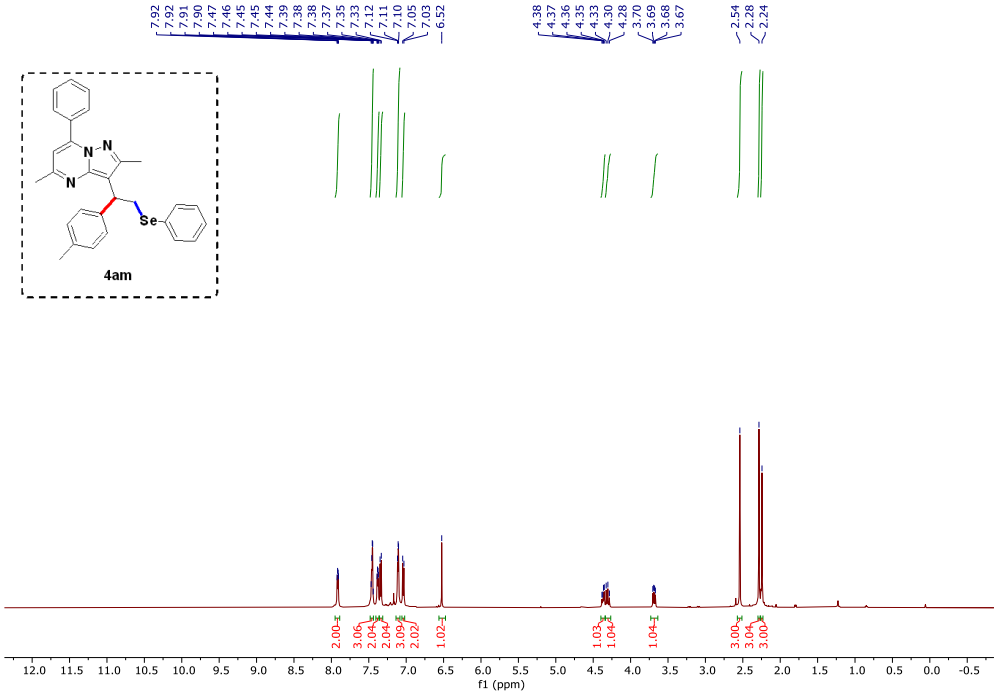


Fig 26: ^{1}H NMR of 4am

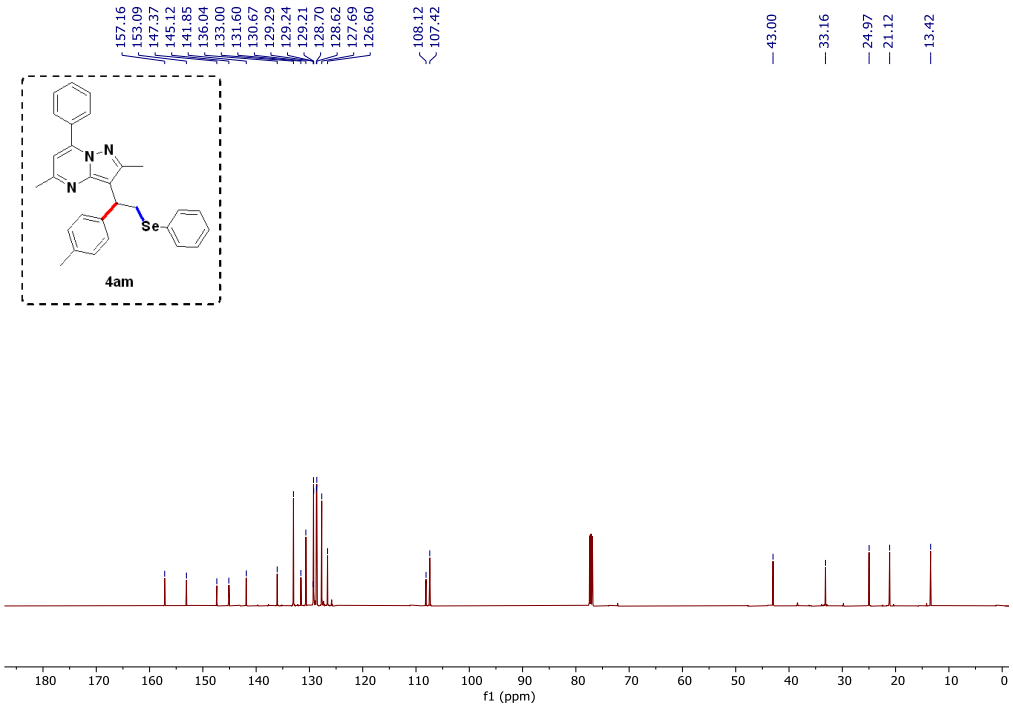


Fig 27: ^{13}C NMR of 4am

4an (^{1}H 500MHz/ ^{13}C{^{1}H} 126MHz-CDCl$_3$)

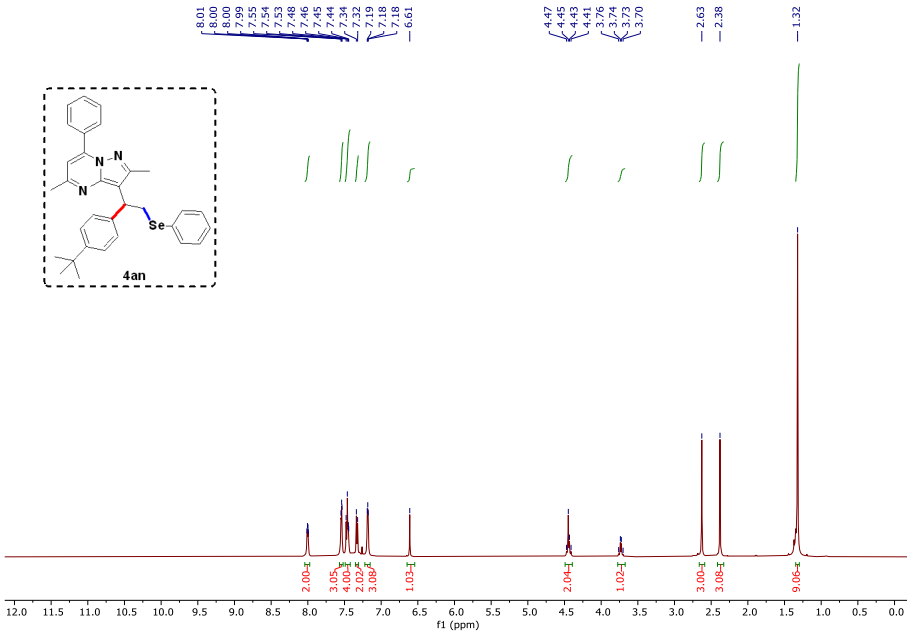


Fig 28: ^{1}H NMR of 4an

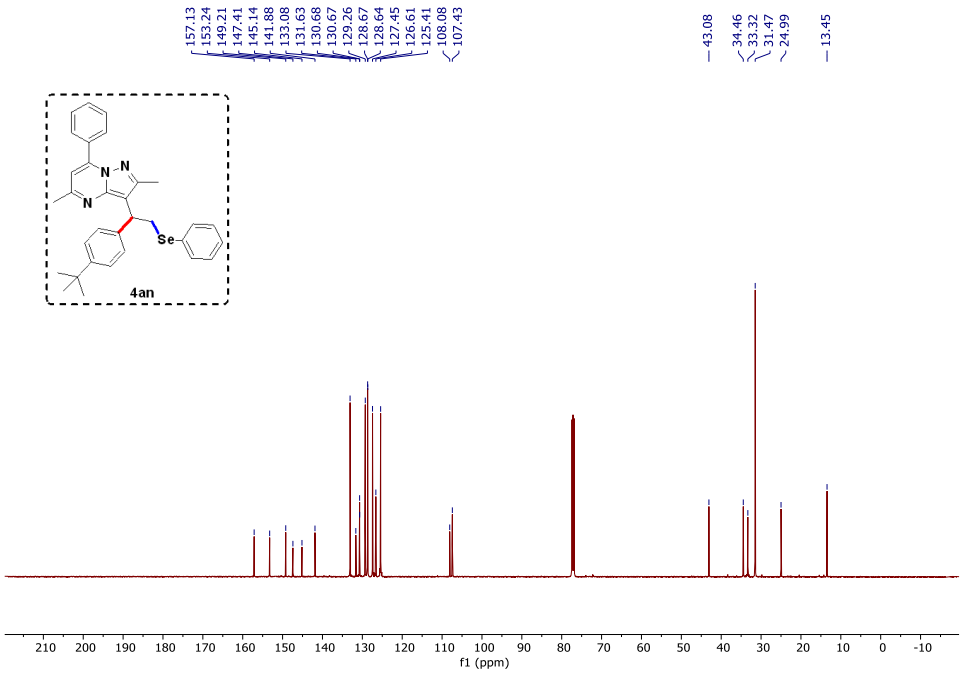


Fig 29: ^{13}C NMR of 4an

4ao (^{1}H 500MHz/ ^{13}C{^{1}H} 126MHz-CDCl$_3$)

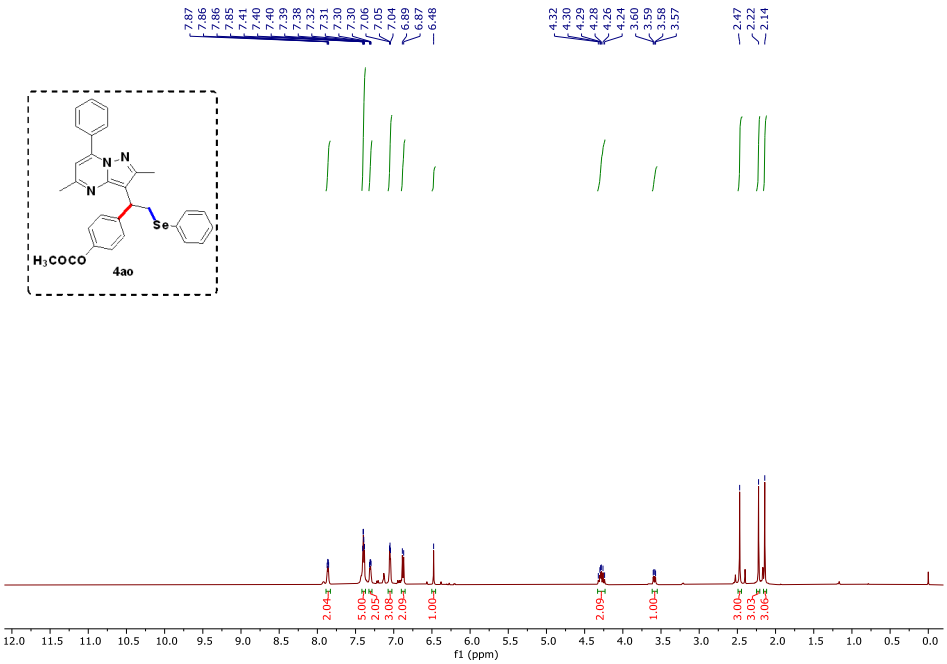


Fig 30: ^{1}H NMR of 4ao

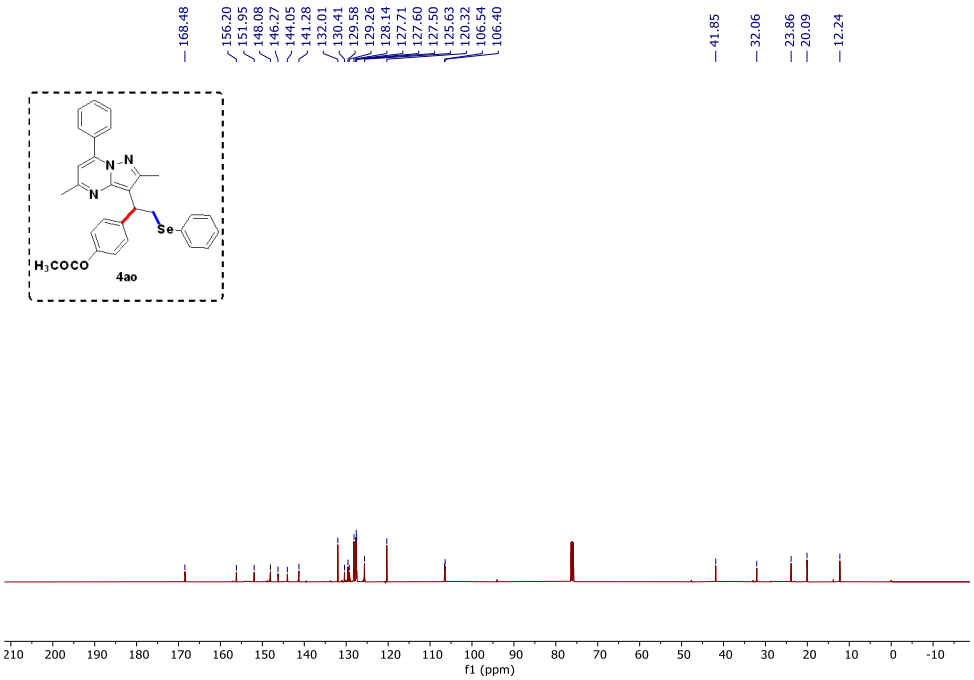


Fig 31: ^{13}C NMR of 4ao

4ap (^{1}H 500MHz/ ^{13}C{^{1}H} 126MHz-CDCl$_3$)

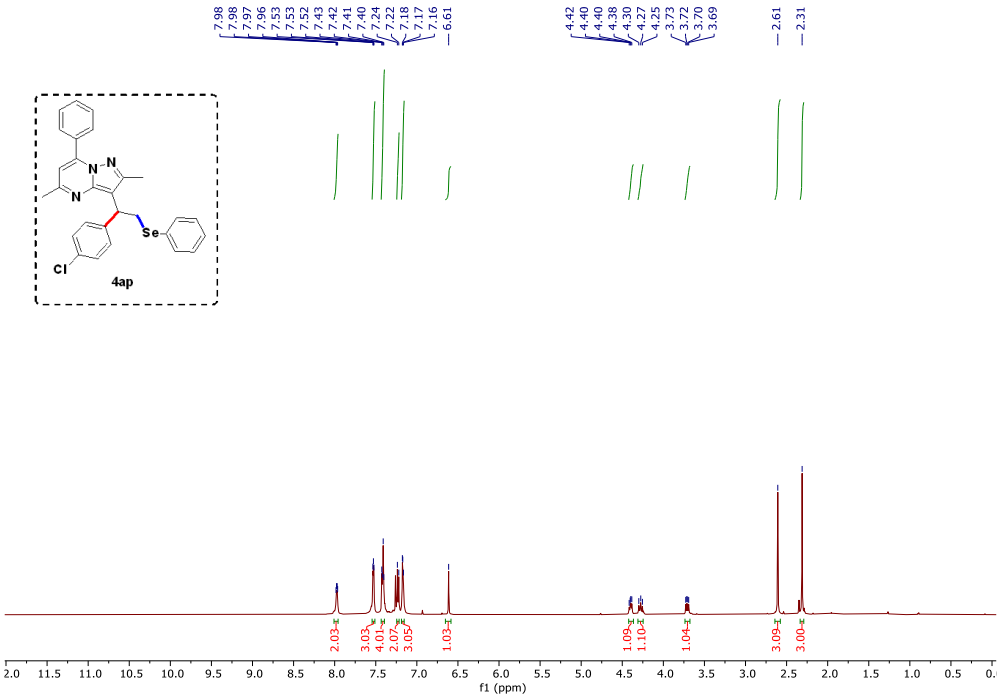


Fig 32: ^{1}H NMR of 4ap

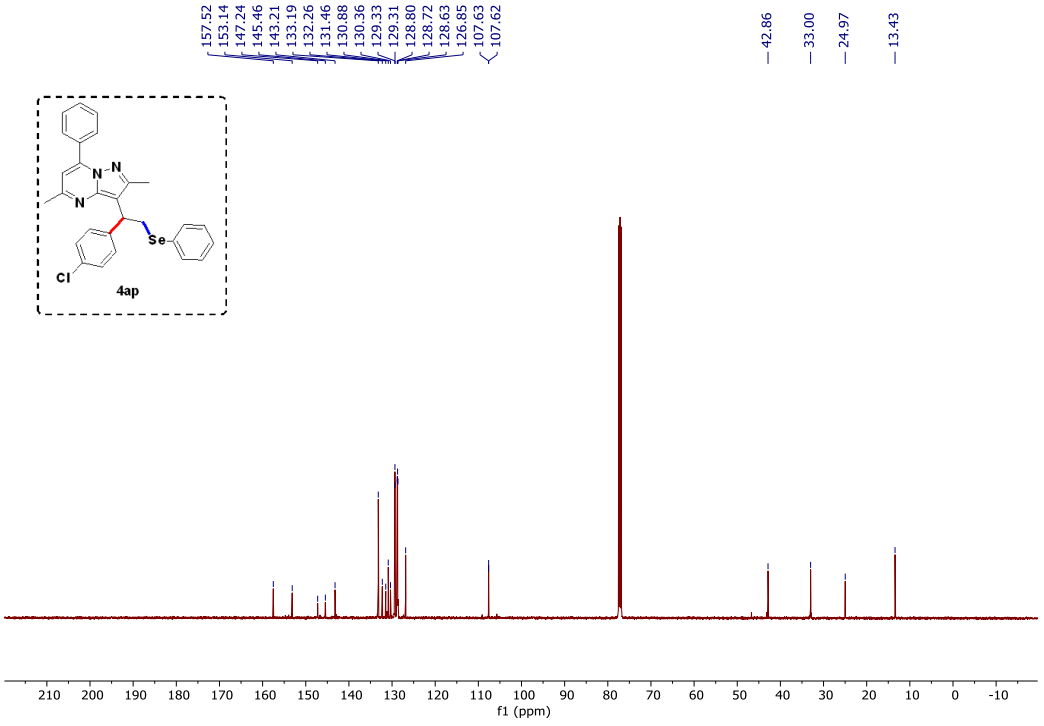


Fig 33: ^{13}C NMR of 4ap

4aq (^{1}H 500MHz/ ^{13}C{^{1}H} 126MHz-CDCl$_3$)

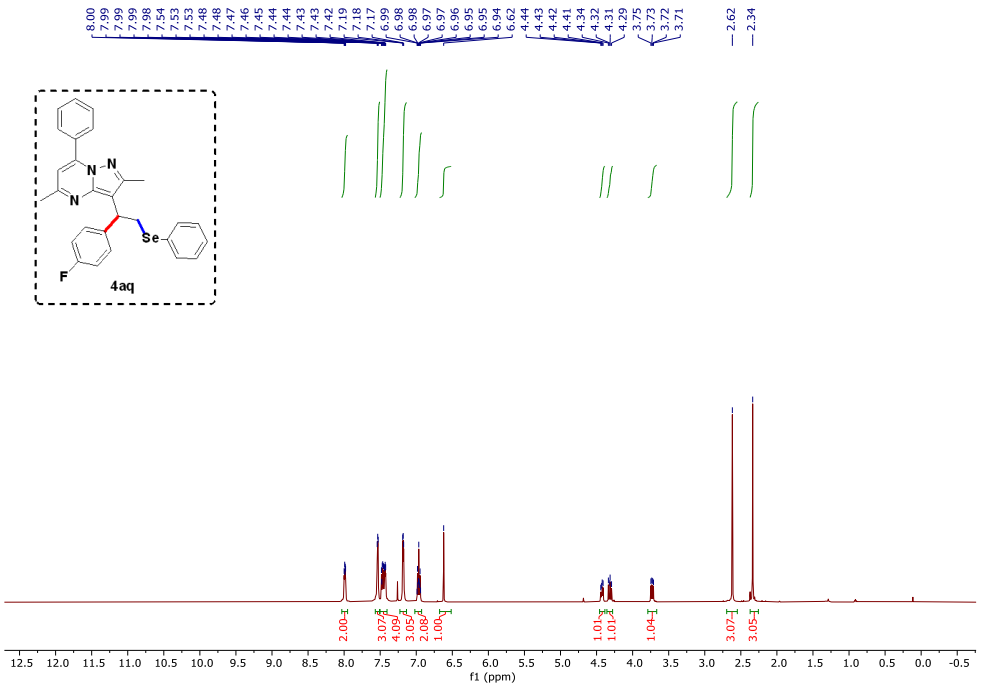


Fig 34: ^{1}H NMR of 4aq

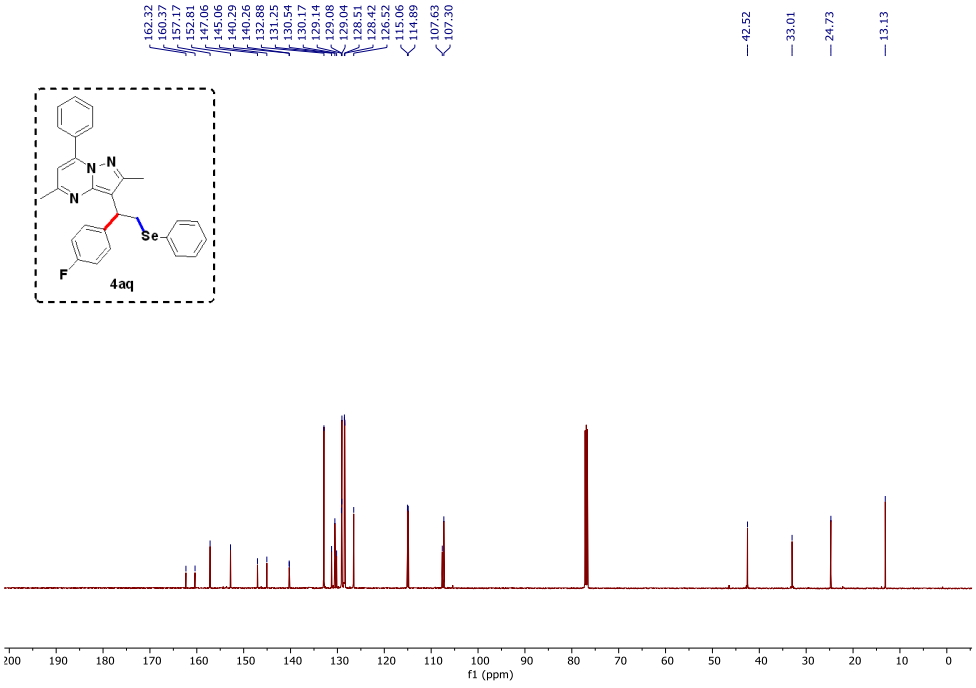


Fig 35: ^{13}C NMR of 4aq

4ar (^{1}H 500MHz/ ^{13}C{^{1}H} 126MHz-$CDCl_3$)

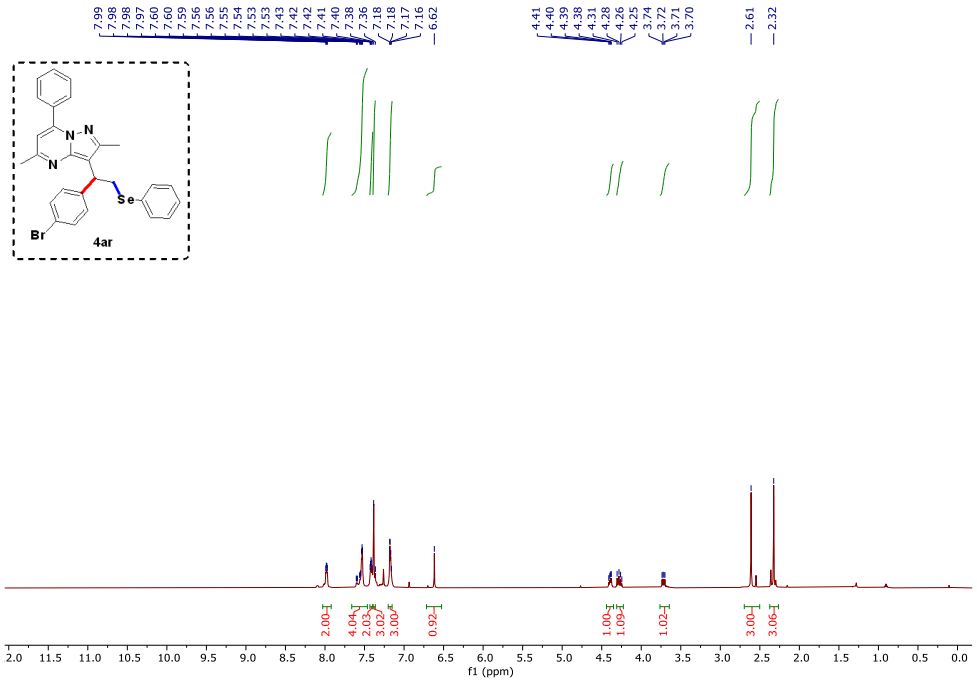


Fig 36: ^{1}H NMR of 4ar

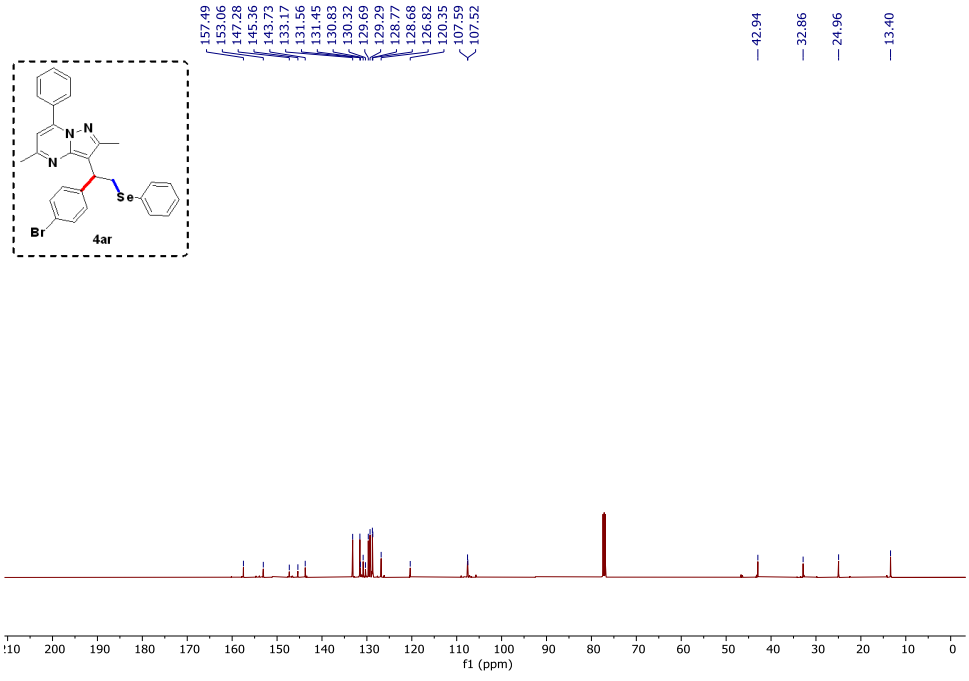


Fig 37: ^{13}C NMR of 4ar

4as (^{1}H 500MHz/ ^{13}C{^{1}H} 126MHz-CDCl$_3$)

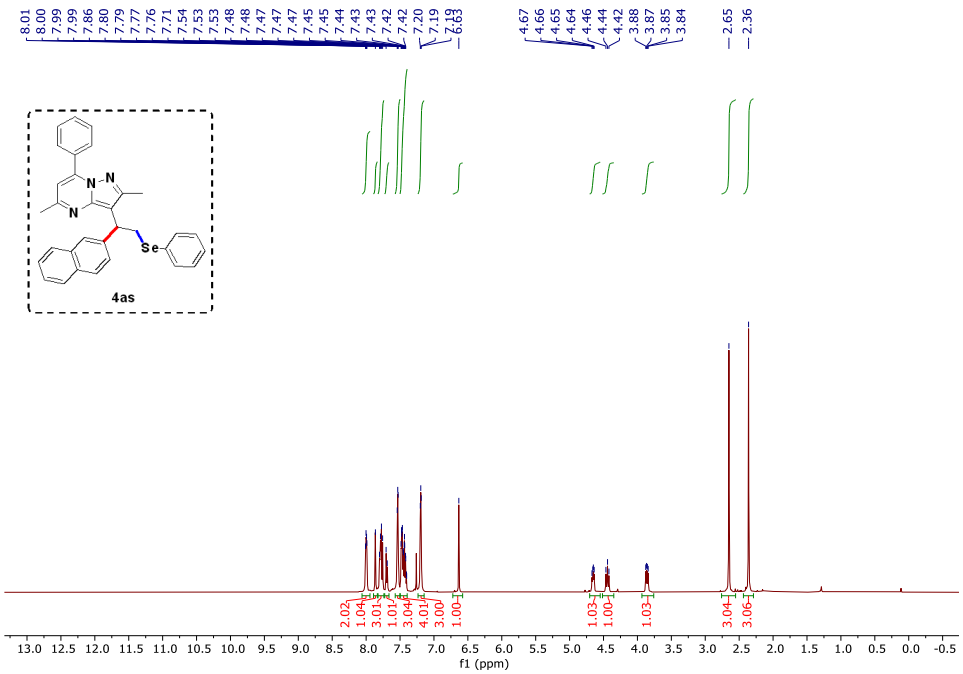


Fig 38: ^{1}H NMR of 4as

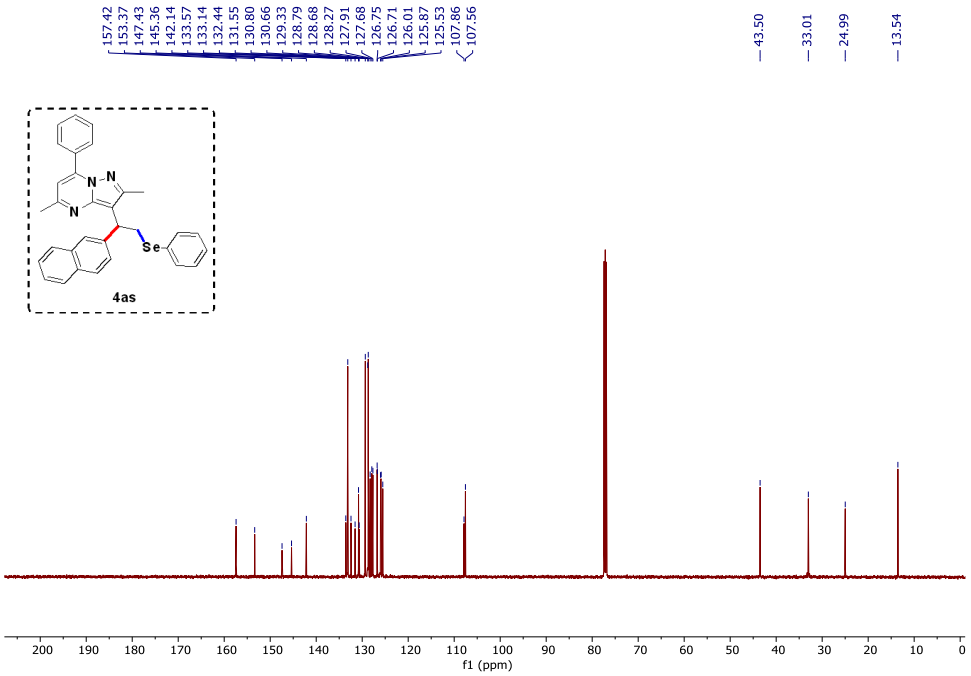


Fig 39: ^{13}CNMR of 4as

4ba (^{1}H 500MHz/ ^{13}C{^{1}H} 126MHz-CDCl$_3$)

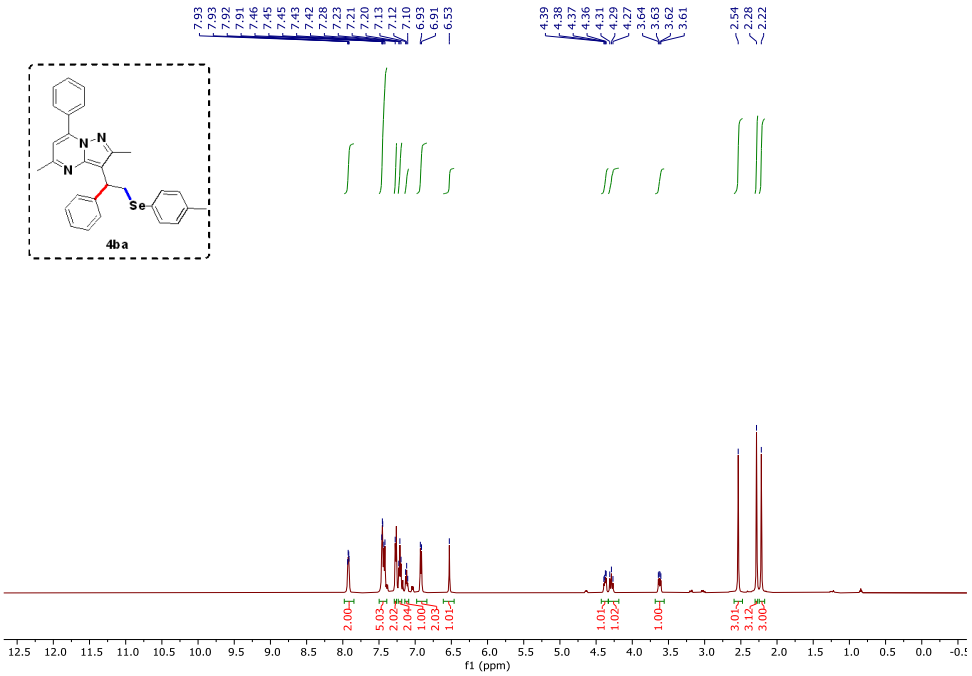


Fig 40: ^{1}H NMR of 4ba

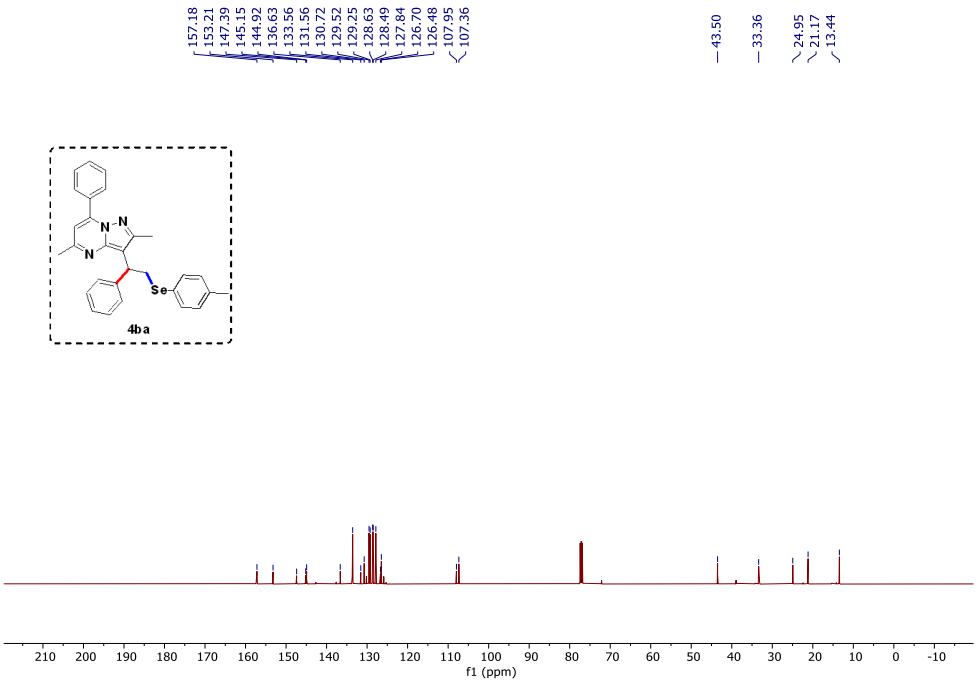


Fig 41: ^{13}C NMR of 4ba

4bb (^{1}H 500MHz/ ^{13}C{^{1}H} 126MHz-CDCl$_3$)

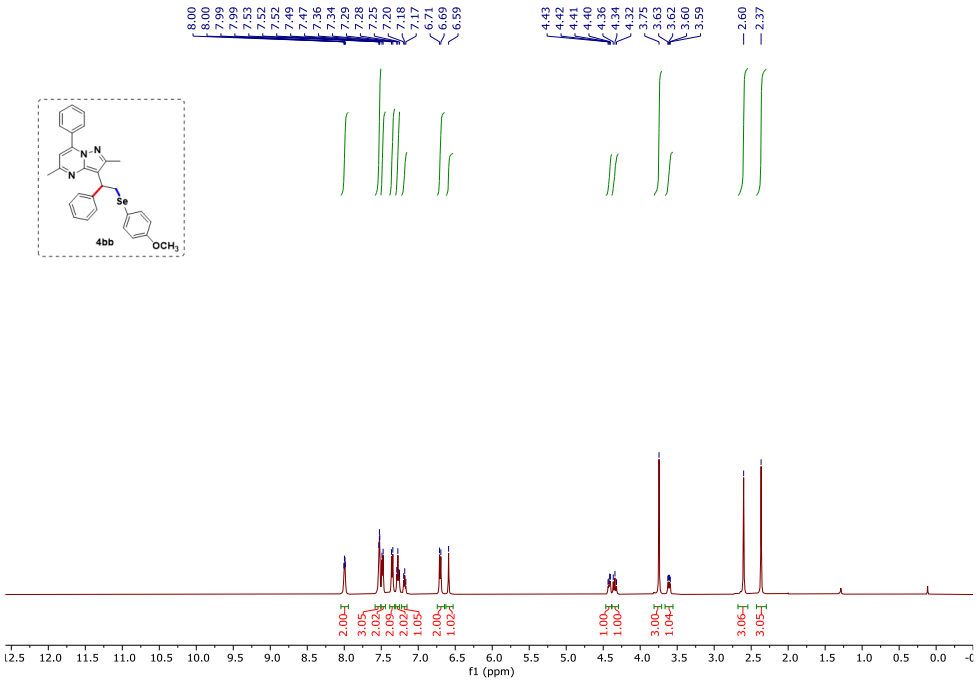


Fig 42: ^{1}H NMR of 4bb

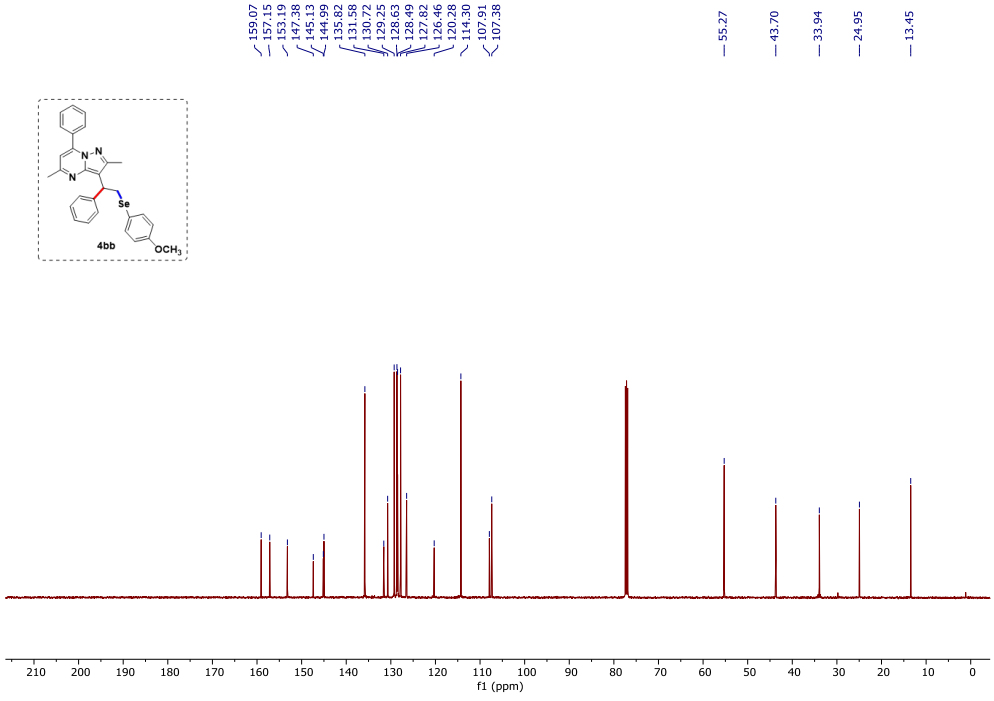


Fig 43: ^{13}CNMR of 4bb

4bc (^{1}H 500MHz/ ^{13}C{^{1}H} 126MHz-CDCl$_3$)

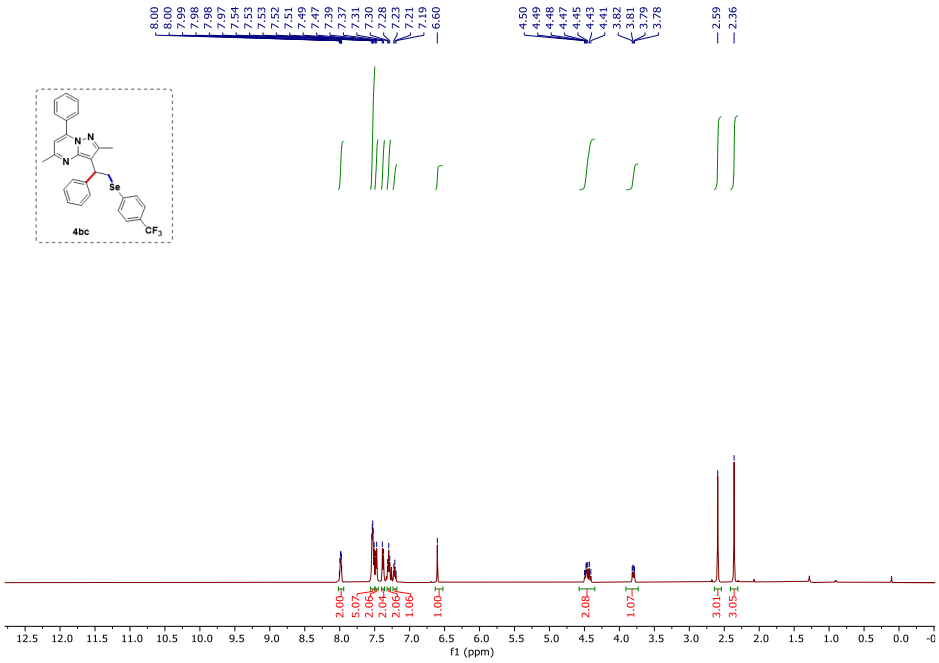


Fig 44: ^{1}H NMR of 4bc

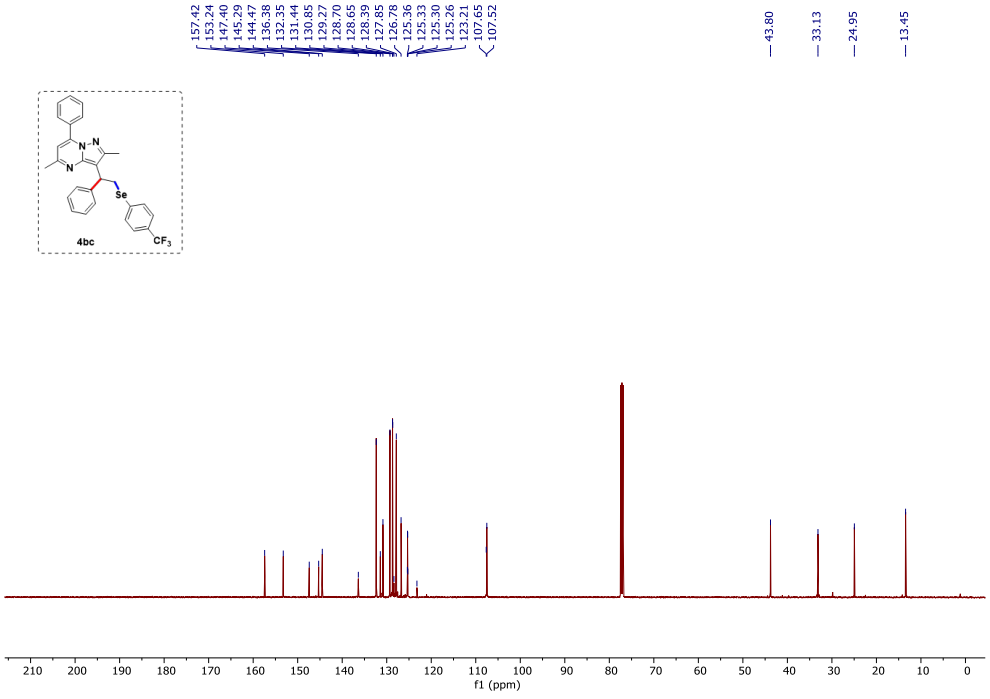


Fig 45: ^{13}C NMR of 4bc

4bd (^{1}H 500MHz/ ^{13}C{^{1}H} 126MHz-CDCl$_3$)

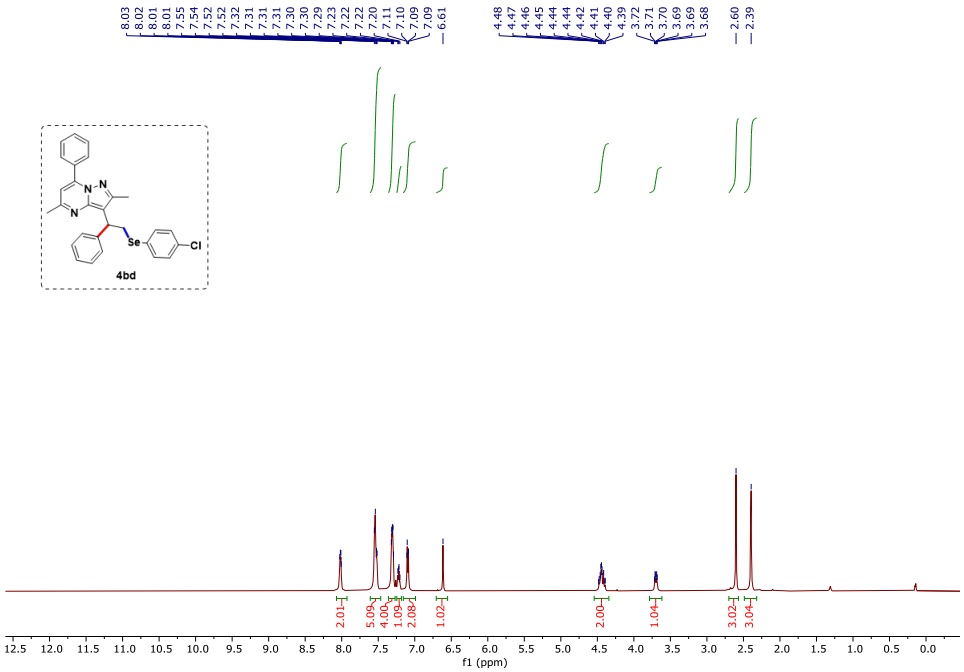


Fig 46: ^{1}H NMR of 4bd

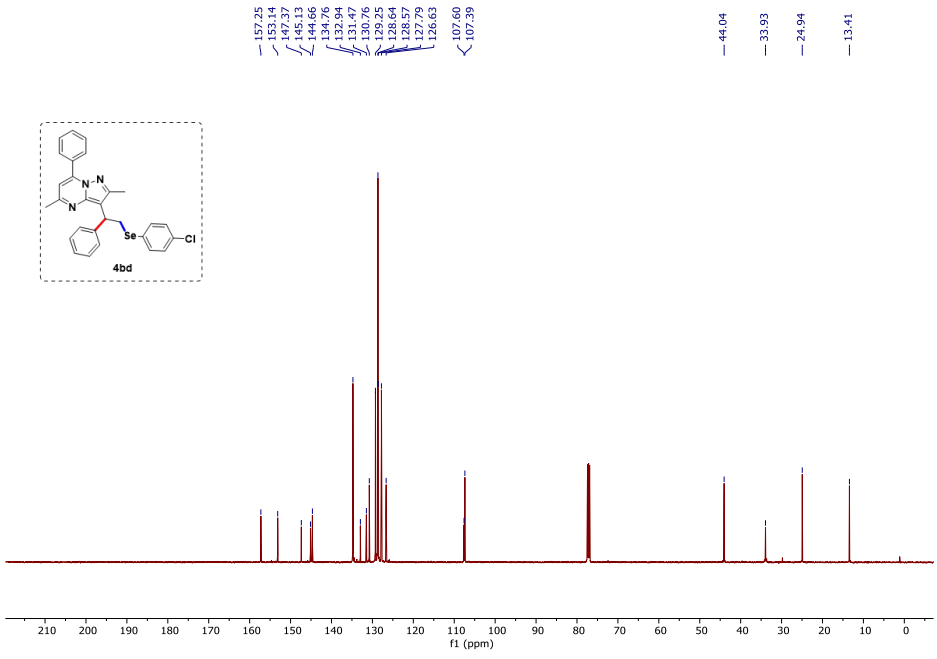


Fig 47: ^{13}C NMR of 4bd

4be (^{1}H 500MHz/ ^{13}C{^{1}H}126MHz-CDCl$_3$)

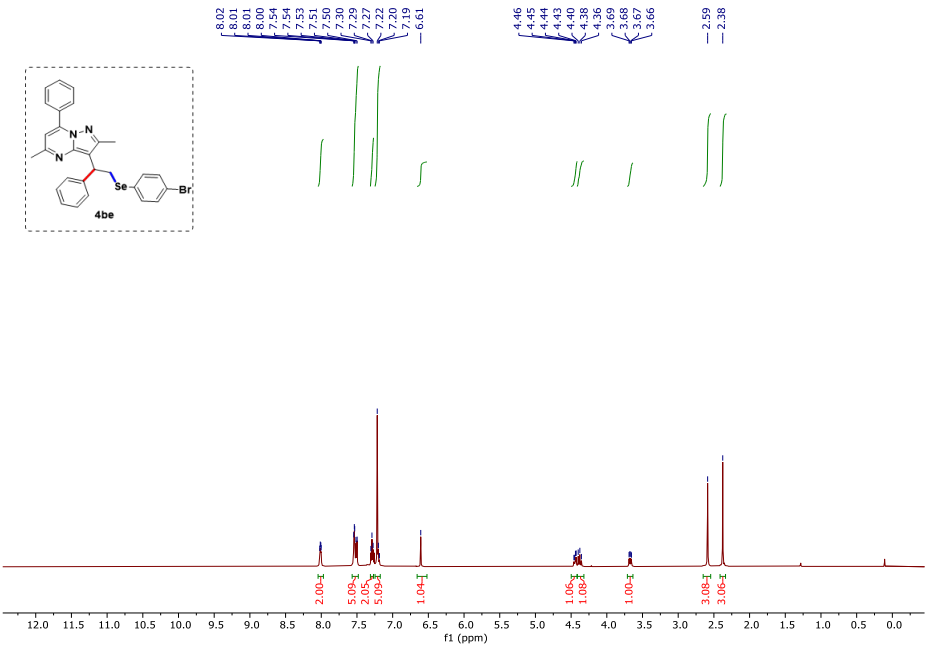


Fig 48: ^{1}H NMR of 4be

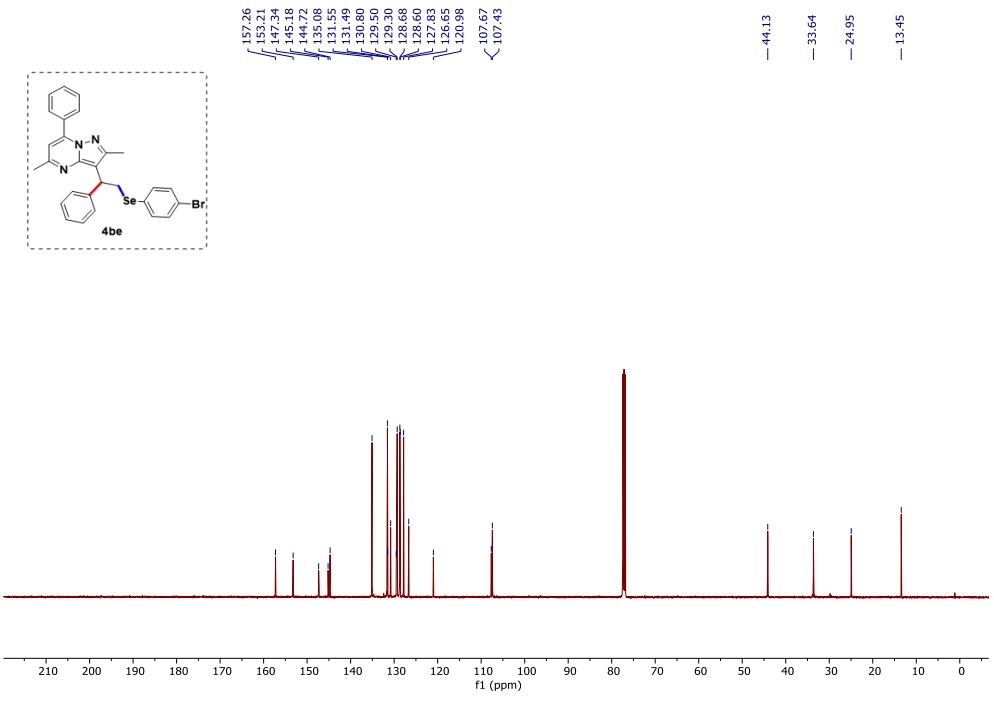


Fig 49: ^{13}C NMR of 4be

Chapter 5: REFERENCES

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