Research Article

SOHAG JOURNAL OF SCIENCES

https://doi.org/10.21608/sjsci.2023.212498.1082

Synthesis and Characterization of Some Novel Selenoazo Derivatives

Amer A. Amer*, Sham M. M. El-Saghier, Bahgat R. M. Hussein

Department of Chemistry, Faculty of Science, Sohag University, Sohag 82524, Egypt
**Email: amer_chem@yahoo.com*

Received: 22nd May 2023, **Revised:** 20th June 2023, **Accepted:** 22nd June 2023
Published online: 24th June 2023

Abstract: A novel series of Se-heterocyclic compounds, which containing azo-dye and organoselenium moieties, have been synthesized by the reaction of 4,6-diamino-2-(methylselanyl)pyridine-3-carbonitrile (**1**) with aromatic diazonium chloride salts. Furthermore, oxobutanamide **3** was obtained *via* N-acetylation of methylselanyl pyridine **1** by ethyl acetoacetate. Product **3** was used as a starting material to synthesize aryl hydrazones **4a** and **4b**. However, an unprecedented series of thiapyridine derivatives **7a** and **7b** was produced through a one-pot multicomponent reaction of methylselanyl pyridine **1** with chloroacetyl chloride and thiophenol derivatives.

Keywords: pyridine, azo dye, methylselanyl, oxobutanamide, Arylhydrazones, thiapyridine, multi-component.

1. Introduction

Heterocyclic azo dyes have many excellent properties, and are an essential class for polyester fiber dyes, also in non-textile industries such as nonlinear optical systems, phototherapy, and lasers [1]. In addition, they have important biological activities such as anticancer, cytotoxicity, antimicrobial, anti-tuberculosis, antifungal, and agricultural pesticides [2, 3]. Besides the chemical utility of selenium compounds, they have broad pharmacological and biological activities, for instance; antifungal activity such as *Aspergillus niger*, *Aspergillus*, and *Candida albicans*, antibacterial such as: *Staphylococcus aureus* as gram-positive bacteria, and Escherichia coli as gram-negative bacteria [4, 5], antiviral [6], anti-inflammatory [7], and anti-oxidant effects [8]. On the other hand, the biological activity of azo dye compounds is elevated when they contain organoselenium moiety. For example, the azo dye contains the selenium compound such as selenopheno **A** characterized antioxidant properties [5], while selenocyanate **B** has antibacterial activity (**Figure 1**). From the above and in continuation of our previous work [10-15], herein, we decided to synthesize some novel azo compounds containing an organoselenium moiety from available material in anticipation of the expected interesting biological activities.

2. Results and discussion

Herein, we successfully synthesized some novel azo dye compounds containing organoselenium moiety **2a-c** using a simple and inexpensive method with high yield *via* the reaction of 4,6-diamino-2-(methylselanyl)pyridine-3-carbonitrile (**1**) [16] with diazonium chloride salts of aromatic amines namely, *p*-methoxyaniline, *p*-chloroaniline and α-naphthylamine in pyridine at 0 ℃ as shown in ***(Scheme 1)***. The structure of azo dye **2a-c** may be has another two tautomeric forms **2´a-c** and **2´´a-c** ***(Scheme 1)***. All the chemical structures of the novel derivatives **2a-c** were confirmed by their elemental and spectral (^{1}H NMR, ^{13}C NMR, IR) analyses. The IR spectrum of product **2a** showed absorption bands corresponding to amino groups at 3456, 3343, and 3212 cm^{-1}, CH aromatic at 3010 cm^{-1}, CH aliphatic at 2957 cm^{-1} in addition to the C≡N group at 2205 cm^{-1}. Its ^{1}H-NMR spectrum showed the absence of the singlet signal characteristic of $CH_{pyridyl}$, While it displayed the presence of a broad signal corresponding to NH at 8.81 ppm, multiplet signals for NH, and two aromatic protons at 7.96-7.95 ppm, broad signals corresponding to NH_2 at 7.73 ppm, doublet signals for equivalent aromatic protons at 7.03 ppm, beside

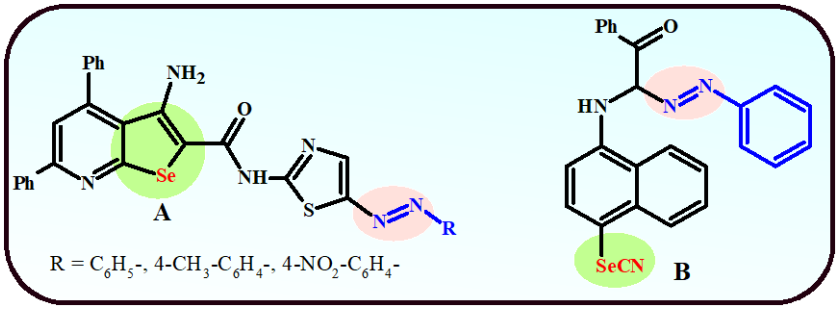
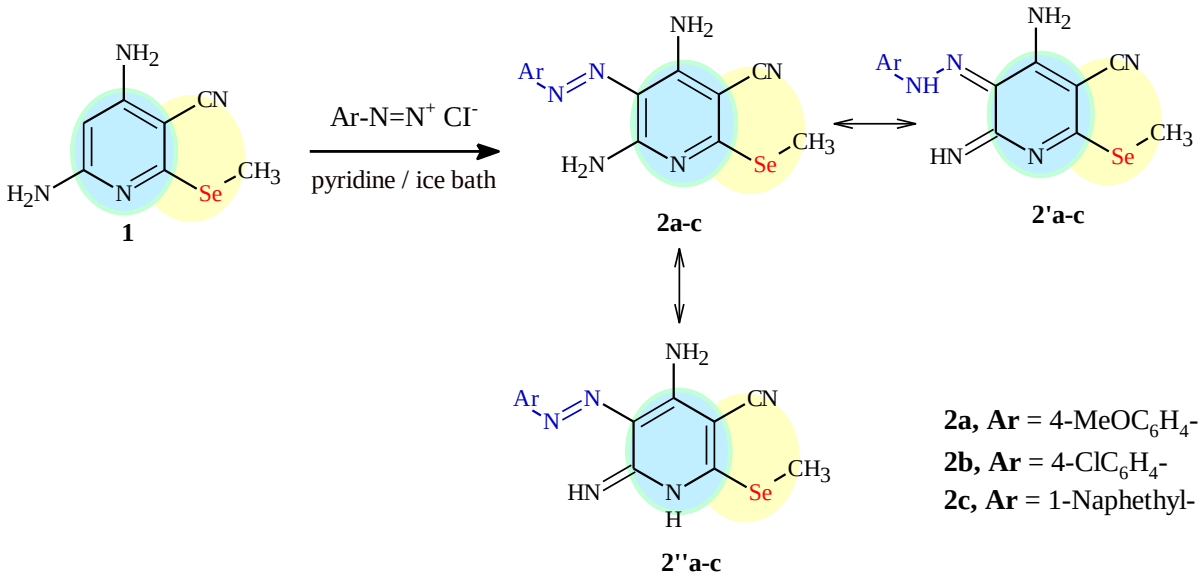


Fig. 1: Selected biologically active organoselenium compounds.

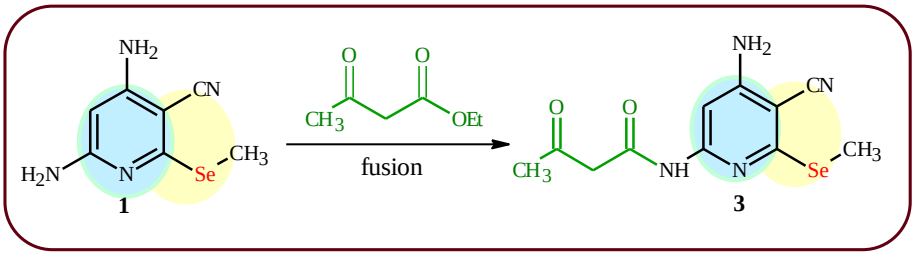


Scheme 1: Synthesis of selenoazo compounds **2a-c**

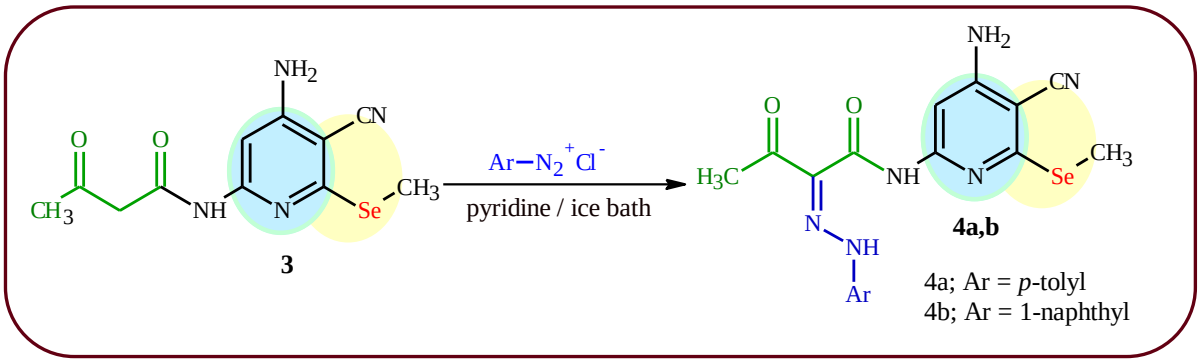
two singlet signals of OCH_3 and $SeCH_3$ protons at 3.84 and 2.47 ppm, respectively. Its ^{13}C NMR spectrum showed three signals corresponding to cyano, methoxy, and $SeCH_3$ groups at 116.87, 55.97, and 6.38 ppm, respectively, while sp^2 carbons signals appear at 162.97, 160.98, 154.35, 152.56, 146.95, 124.13, 114.81, 113.55, 83.45 ppm.

N-acylation of methylselanyl pyridine **1** by ethyl acetoacetate as the acyl source in presence of piperidine as the basic catalyst without solvent, fusion for 30 min. afforded derivative **3** ***(Scheme 2)***. The IR spectrum of derivative **3** exhibited absorption bands for amino groups (NH and NH_2) at 3333, 3317, and 3202 cm^{-1}, bands of aromatic and aliphatic CH groups 3042, and 2930 cm^{-1} respectively, besides three bands corresponding to cyano and two carbonyl groups at 2198, 1709 and 1687 cm^{-1}, respectively. While its ^1H NMR spectrum showed three singlet signals for NH, $CH_{pyridyl,}$ and NH_2 groups at 10.28, 7.33 and 6.97 ppm, new two singlet signals appeared at 3.67 and 2.45 ppm for CH_2 and $COCH_3$ protons, also singlet signal at 2.19 ppm due to $SeCH_3$ protons. Its ^{13}C NMR spectrum exhibited new signals at 203.05, 166.73, 52.70, and 30.59 ppm which were assigned to two carbonyl groups, CH_2 and CH_3 carbons, in addition to three signals at 116.31, 94.17, and 6.24 ppm corresponding to cyano, $CH_{pyridyl,}$ and $SeCH_3$ carbons, respectively. Whereas the aromatic carbons appeared at 158.87, 158.67, 152.93, and 88.36 ppm. Its Dept-135 NMR spectrum showed three signals in a positive direction at 94.07, 30.61, 6.24 ppm for $CH_{pyridyl}$, $CH_{3,}$ and $SeCH_3$ groups respectively, while CH_2 carbon appeared in a negative direction at 52.71 ppm.

The reaction of oxobutanamide **3** with the respective diazonium chlorides of *p*-toluidine and *α*-naphthylamine in pyridine at 0 ℃ takes place on the active methylene group instead of the pyridine ring to afford aryl hydrazones **4a** and **4b** ***(Scheme 3)***. The IR spectrum of arylhydrazone **4a** indicated absorption bands at 3352, 3245, and 3159 cm^{-1} due to NH_2 and NH groups, $CH_{arom.}$ at 3038 cm^{-1}, $CH_{aliph.}$ at 2934 cm^{-1}, nitrile group at 2205 cm^{-1} and two carbonyl groups at 1705 and 1673 cm^{-1}. Its ^1H NMR spectrum showed the disappearance of the methylene group while exhibiting two singlet signals for two NH protons at 14.04, 11.63 ppm, multiplet signals appeared at 7.41-7.14 ppm for protons of CH_{arom}, $CH_{pyridy,}$ and NH_2, in addition to $2CH_3$ and $SeCH_3$ protons as two singlet signals at 2.41 and 2.32 ppm, respectively. Its ^{13}C NMR illustrated an increase in the aromatic signals, which appeared at 159.20, 158.62, 151.91, 139.68, 135.55, 130.58, 125.84, 116.20, and 88.64 ppm, besides seven signals for two carbonyl groups, nitrile, $CH_{pyridyl}$, $2CH_{3,}$ and $SeCH_3$ carbons appeared at 198.98, 162.65, 116.54, 95.04, 26.30, 20.98 and 6.22 ppm, respectively.

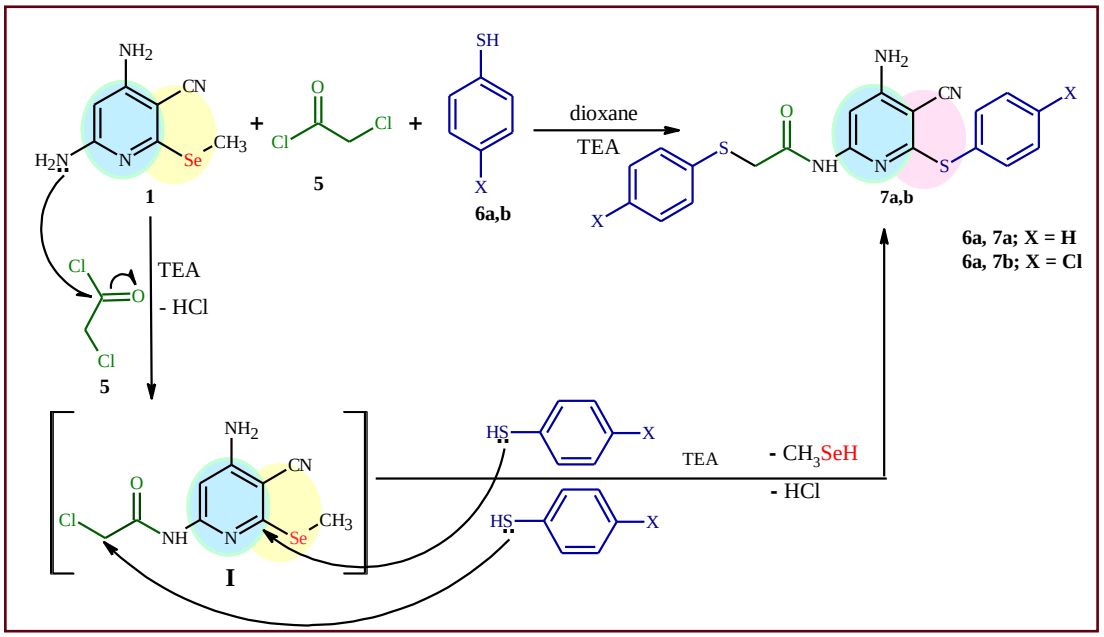


Scheme 2: N-acylation of methylselanyl pyridine **1**



Scheme 3: Synthesis of Arylhydrazones **4a** and **4b**

One-pot, the three-component reaction of methylselanyl pyridine **1**, chloroacetyl chloride **5**, thiophenol (**6a**), and/or *p*-chlorothiophenol (**6b**) in the presence of catalytic amounts of TEA under reflux in dioxane for 4 hrs. afforded the thiapyridine derivatives **7a** and **7b**. The reaction mechanism for the formation of products **7a** and **7b** was proposed to initiate by a nucleophilic attack of the amino group (has lone pair of electrons) of compound **1** at the active carbonyl group in chloroacetyl chloride **5** producing the intermediate **I**, *via* elimination of HCl molecule. Then, two moles of thiophenol derivative attacked the intermediate **I** to give products **7a** and **7b** *via* the elimination of CH_3SeH and HCl molecules (***Scheme 4***). The chemical structures of the newly synthesized compounds **7a** and **7b** were assured by their spectroscopic (IR, ^{1}H-NMR, ^{13}C-NMR, Dept-135) and elemental analyses. The IR spectrum of derivative **7a** (as an example) showed absorption bands attributed to amino and NH groups at 3428, 3332, and 3203 cm^{-1}, $CH_{arom.}$ and $CH_{aliph.}$ at 3049 and 2988 cm^{-1}, cyano group at 2210 cm^{-1}and carbonyl group at 1682 cm^{-1}. Its ^{1}H NMR spectrum showed the absence of a $SeCH_3$ signal while exhibiting a singlet signal corresponding to NH at 10.26, two phenyl groups appeared as multiplet signals at 7.50-7.42 and 7.37-7.28 ppm, in addition to three singlet signals at 7.21, 7.12 and 3.89 ppm corresponding to $CH_{pyridyl}$, NH_2 and CH_2 protons, respectively. Whereas the ^{13}C NMR spectrum showed an increase in aromatic signals at 160.27, 159.08, 153.09, 135.90, 133.45, 130.66, 129.81, 129.46, 128.99, 128.78, 126.62, and 87.87 ppm, in addition to carbonyl, nitrile, $CH_{pyridyl,}$ and CH_2 carbons appeared at 168.66, 115.54, 95.07 and 37.65 ppm, respectively. Its Dept-135 NMR spectrum showed seven signals in a positive direction at 133.51, 129.82, 129.47, 129.04, 128.79, and 126.67, 95.05 ppm for CH phenyl and $CH_{pyridyl}$ carbons, while CH_2 carbon appeared in the negative direction at 37.65 ppm.



Scheme 4: Probable reaction mechanism for the synthesis of thiapyridine derivatives **7a** and **7b**.

3. Conclusion

Using methylselany pyridine **1** as a starting material, we successfully synthesized a new series of Se-heterocyclic compounds containing both of the azo-dye and organoselenium moieties **2a, c**. In addition, oxobutanamide **3** was obtained and treated with aromatic diazonium chloride salts to give arylhydrazones **4a** and **4b**. Also, a new series of thiopyridine derivatives **7a** and **7b** were prepared *via* a multi-component reaction of methylselanyl pyridine **1**, chloroacetyl chloride, and thiophenol derivatives. We are hoping that all of the synthesized products will give promising antibacterial and anticancer activity if they evaluate against different types of bacterial and human cancer cells.

4. Experimental

All melting points were uncorrected and recorded through the Kofeler melting point apparatus. Any reaction was monitored by TLC plates (silica gel/ UV light (254 nm/365 nm) for visualization). IR spectra were measured (KBr pellets) on a spectrometer FT-IR spectrophotometer. ^{1}H NMR spectra were recorded at 400 M Hz, ^{13}C NMR, and Dept 135 (DMSO-d_6) was recorded at 100 MHz on Bruker Bio Spin AG at Sohag University. Elemental analyses were given on a Perkin-Elmer CHN as an analyzer model.

The general method for the formation of compounds 2a-c:

To a stirred solution of appropriate aromatic amine (2 mmol) namely; *p*-methoxyaniline (0.27 g), *p*-chloroaniline (0.28 g), and/or α-naphthylamine (0.31 g) in 5 mL of conc. HCl, 2 mL of sodium nitrite as an aqueous solution (0.15 g, 2 mmol) was added at 0-5 ºC. The solution of diazonium salt was added with stirring to methylselanyl pyridine **1** (0.5 g, 2 mmol) in pyridine (20 mL) at 0-5 ºC. The reaction mixture was allowed to stand at a low temperature for 20 minutes. Then it was poured into 50 mL water. The formed precipitate was filtered off, washed with distilled water, dried, and crystallized from dioxane.

4,6-Diamino-5-[4-methoxyphenyl)diazenyl]-2-(methylselanyl) pyridine-3-carbonitrile (2a):

Brown, yield 0.57 g (88%), mp170-172 ºC; FT-IR (ATR) ν_{max}: 3456, 3343, 3212 (NH_2 and 2NH), 3010 ($CH_{arom.}$), 2957 ($CH_{aliph.}$), 2205 (C≡N) cm^{-1}; ^{1}H NMR: δ 8.81 (br, 1H, NH), 7.96-7.95 (m, 3H, NH+ $CH_{arom.}$), 7.73 (br, 2H, NH_2), 7.03 (d, 2H, *J* = 5.9 Hz, $CH_{arom.}$), 3.84 (s, 3H, OCH_3) 2.47 (s, 3H, $SeCH_3$) ppm; ^{13}C NMR:δ 162.97, 160.98, 154.35, 152.56, 146.95, 124.13, 116.87 (CN), 114.81, 113.55, 83.45, 55.97 (OCH_3), 6.38 ($SeCH_3$) ppm; *Anal*. Calcd. For $C_{14}H_{14}N_6OSe$ (361.26): C, 46.55, H, 3.91, N, 3.26%. Found: C, 46.72, H, 3.79, N, 3.44%.

4,6-Diamino-5-[(4-chlorophenyl)diazenyl]-2-(methylselanyl) pyridine-3-carbonitrile (2b):

Dark orange, yield 0.68 g (85%), mp. 180-182ºC; FT-IR (ATR) ν_{max}: 3463, 3391, 3335, 3210 (NH_2 and 2NH), 3088 ($CH_{arom.}$), 2971($CH_{aliph.}$), 2204 (C≡N), 1627 (C=N) cm^{-1}; ^{1}H NMR: δ 8.92 (br, 1H, NH), 8.02-7.89 (m, 4H, NH+$CH_{arom.}$), 7.52-7.50 (m, 3H, CH_{arom}+ NH_2), 2.48 (s, 3H, $SeCH_3$) ppm; ^{13}C NMR:δ 164.60, 154.25, 153.08, 151.45, 133.95, 129.54, 124.12, 116.74 (CN), 114.17, 83.34, 6.50 ($SeCH_3$) ppm; *Anal*. Calcd. For $C_{13}H_{11}ClN_6Se$ (365.67): C, 42.70, H, 3.03, N, 22.98 %. Found: C, 42.58, H, 3.12, N, 22.78 %.

4,6-Diamino-2-(methylselanyl)-5-[(naphthalen-1-yl)diazenyl] pyridine-3-carbonitrile (2c):

Black, yield 0.73 g (87%), mp.178-180 ºC; FT-IR (ATR) ν_{max}: 3465, 3378, 3323, 3196 (NH_2 and 2NH), 3050 ($CH_{arom.}$), 2949 ($CH_{aliph.}$), 2203 (C≡N), 1593 (C=N) cm^{-1}; ^{1}H NMR: δ 9.07 (br, 1H, NH), 8.45 (br, 1H, NH), 8.12-8.02 (m, 5H, $CH_{arom.}$+NH_2), 7.69-7.62 (m, 4H, $CH_{arom.}$), 2.51 (s, 3H, $SeCH_3$) ppm; ^{13}C NMR: δ 164.68, 154.55, 152.74, 147.95, 134.39, 129.80, 129., 128.78, 127.52, 126.84, 126.56, 122.49, 116.70 (CN), 115.33, 113.17, 83.55, 6.59 ($SeCH_3$) ppm; *Anal*. Calcd. For $C_{17}H_{14}N_6Se$ (381.29): C, 53.55, H, 3.70, N, 22.04 %. Found: C, 53.74, H, 3.58, N, 22.13 %.

Synthesis of *N*-[4-amino-5-cyano-6-(methylselanyl)pyridin-2-yl]-3-oxobutanamide (3):

An equimolar mixture of methylselanyl pyridine **1** (0.5 g, 2 mmol), ethyl acetoacetate (0.28 g, 2 mmol) and piperidine (0.18 g, 1 mmol) was heated for about 30 min. The reaction mixture was washed with dry ether; the formed precipitate **3** was gathered and crystallized from ethanol.

Pale yellow, yield 0.6 g (89%), mp. dec. 246-248 ºC; FT-IR (ATR) ν_{max}: 3333, 3317, 3202 (NH_2 and NH), 3042 ($CH_{arom.}$), 2930 ($CH_{aliph.}$), 2198 (C≡N), 1709 (C=O), 1687 (C=O_{amidic}) cm^{-1}; ^{1}H NMR: δ 10.28 (s, 1H, NH), 7.33 (s, 1H, $CH_{pyridyl}$), 6.97 (s, 2H, NH_2), 3.67 (s, 2H, CH_2), 2.45 (s, 3H, CH_3), 2.19 (s, 3H, $SeCH_3$) ppm; ^{13}C NMR: δ 203.05 (C=O), 166.73 (C=O_{amidic}), 158.87, 158.67, 152.93, 116.31, (CN), 94.17($CH_{pyridyl}$), 88.36, 52.70 (CH_2), 30.59 ($COCH_3$), 6.24 ($SeCH_3$) ppm; Dept-135 NMR: δ 94.07 ($CH_{pyridyl}$), 52.71 (CH_2, exchangeable), 30.61 ($COCH_3$), 6.24 ($SeCH_3$) ppm; *Anal*. Calcd. For $C_{11}H_{12}N_4O_2Se$ (311.19): C, 42.45, H, 3.89, N, 18.00%. Found: C, 42.57, H, 3.68, N, 18.11%.

The general method for the formation of compounds 4a and 4b:

To a stirred solution of appropriate aromatic amine (1.6 mmol) namely, *p*-toluidine (0.17 g), α-naphthylamine (0.229 g) in 5 mL of conc. HCl at 0-5 ºC, HCl, 2 mL of sodium nitrite as an aqueous solution (0.11 g, 1.6 mmol) was added at 0-5 ºC. The solution of the formed diazonium salt was added with stirring to the solution of compound **3** (0.5 g, 1.6 mmol) in 20 mL of pyridine. The reaction mixture was allowed to stand for 20 minutes in an ice bath. Then it was poured into 50 mL water. The formed precipitate was filtered off, washed with distilled water, dried, and crystallized from ethanol.

N-[4-Amino-5- cyano -6-(methylselanyl)pyridin-2-yl]-2-[2-(4-methylphenyl)hydrazinylidene]-3-oxobutanamide (4a):

Dark yellow, yield 0.64 g (93%), mp. 281- 282ºC; FT-IR (ATR) ν_{max}: 3352, 3245, 3159 (NH_2 and 2NH), 3038 ($CH_{arom.}$), 2934 ($CH_{aliph.}$), 2205 (C≡N), 1705 (C=O), 1673 (C=O_{amidic}) cm^{-1}, ^{1}H NMR: δ 14.04 (s, 1H, NH), 11.63 (s, 1H, NH), 7.41-7.14 (m, 7H, $CH_{arom.}$+ $CH_{pyridyl}$ + NH_2), 2.41 (s, 6H, $COCH_3$+ $SeCH_3$), 2.32 (s, 3H, CH_3) ppm; ^{13}C NMR: δ 198.98 (C=O), 162.65 (C=O_{amidic}), 159.20, 158.62, 151.91, 139.68, 135.55, 130.58, 125.84, 116.54 (CN), 116.20, 95.04 ($CH_{pyridyl}$), 88.64, 26.30 ($COCH_3$), 20.98 (CH_3), 6.22 ($SeCH_3$) ppm; *Anal*. Calcd. For

$C_{18}H_{18}N_6O_2Se$ (429.33): C, 50.36, H, 4.23, N, 19.57%. Found: C, 50.44, H, 4.53, N, 19.43%.

N-[4-Amino-5-cyano-6-(methylselanyl)pyridin-2-yl]-2-[2-(naphthaalene-1-yl)hydrazinylid-ene]-3-oxobutanamide (4b):

Dark red, yield 0.65 g (87%), mp. > 300 ºC; FT-IR (ATR) ν_{max}: 3356, 3239, 3166 (NH_2 and 2NH), 3061 ($CH_{arom.}$), 2924 ($CH_{aliph.}$), 2205 (C≡N), 1701 (C=O), 1683 ($C{=}O_{amidic}$) cm^{-1}; ^1H NMR: δ 15.07 (s, 1H, NH), 11.71 (s, 1H, NH), 8.01-7.60 (m, 7H, $CH_{arom.}$), 7.43 (s, 1H, $CH_{pyridyl}$), 7.12 (s, 2H, NH_2), 2.55 (s, 3H, $COCH_3$), 2.41(s, 3H, $SeCH_3$) ppm; *Anal*. Calcd. For $C_{21}H_{18}N_6O_2Se$ (465.36): C, 54.20, H, 3.90, N, 18.06%. Found: C, 54.05, H, 3.79, N, 18.14%.

General method for formation of compounds 7a and 7b: An equimolar amount of methylselanyl pyridine **1** (0.5 g, 2 mmol) and chloroacetyl chloride (0.24 g, 2 mmol) in (30 ml) dioxine was stirring for 30 min then 2 mmol (**Method A**) and/or 4 mmol (**Method B**) of an appropriate thiol namely: thiophenol (0.24 g, **Method A** and/or 0.48 g, **Method B**) and/or *p*-chlorothiophenol (0.31 g, **Method A** and/or 0.62 g, **Method B)** and TEA (0.22 g, 2 mmol) was added gradually in about 15 min. Then, the reaction mixture was refluxed for 4 hrs (monitored by using TLC). The excess solvent was evaporated under a vacuum and the formed precipitate was filtered off, and recrystallized from ethanol to give the desired product 7a and/or 7b.

N-[4-amino-5-cyano-6-(phenylsulfanyl)pyridin-2-yl]-2-(phenylsulfanyl)acetamide (7a):

Yellow, yield (36% method **A**; 75% method **B**), mp. 190-192 ºC; FT-IR (ATR) ν_{max}: 3428, 3332, 3203 (NH_2 and NH), 3049 ($CH_{arom.}$), 2988 ($CH_{aliph.}$), 2210 (C≡N), 1682 (C=O) cm^{-1}, ^1H NMR: δ 10.26 (s, 1H, NH), 7.50-7.42 (m, 5H, $CH_{arom.}$), 7.37-7.28 (m, 5H, $CH_{arom.}$), 7.21 (s, 1H, $CH_{pyridyl}$), 7.12 (s, 2H, NH_2), 3.89 (s, 2H, CH_2) ppm; ^{13}C NMR: δ 168.66 (C=O), 160.27, 159.08, 153.09, 135.90, 133.45, 130.66, 129.81, 129.46, 128.99, 128.78, 126.62, 115.54 (CN), 95.07 ($CH_{pyridyl}$), 87.87, 37.65 (CH_2) ppm; Dept-135 NMR: δ 133.51 (CH_{phenyl}), 129.82 (CH_{phenyl}), 129.47 (CH_{phenyl}), 129.04 (CH_{phenyl}), 128.79 (CH_{phenyl}), 126.67 (CH_{phenyl}), 95.05 ($CH_{pyridyl}$), 37.65 (CH_2, exchangeable); *Anal*. Calcd. For $C_{20}H_{16}N_4OS_2$ (392.49): C, 61.20, H, 4.11, N, 14.27%. Found: C, 61.09, H, 4.29, N, 14.42%.

N-{4-Amino-6-[(4-chlorophenyl)sulfanyl]-5-cyanopyridin-2-yl}-2-[(4-chlorophenylsulfanyl]acetamide (7b):

Beige, yield (37% method **A**; 78% method **B**), mp. 218-220 ºC; FT-IR (ATR) ν_{max}: 3446, 3326, 3202 (NH_2 and NH), 3049 ($CH_{arom.}$), 2208 (C≡N), 1686 (C=O) cm^{-1}; ^1H: δ 10.19 (s, 1H, NH), 7.50 (s, 4H, $CH_{arom.}$), 7.38 (s, 5H, CH_{arom+} $CH_{pyridyl}$), 7.08 (s, 2H, NH_2), 3.90 (s, 2H, CH_2) ppm; ^{13}C NMR: δ 168.45 (NC=O), 159.98, 159.10, 153.05, 135.45, 135.13, 134.05, 131.33, 130.53, 129.77, 129.39, 129.33, 115.44 (CN), 95.11 ($CH_{pyridyl}$), 87.43, 37.70 (CH_2) ppm. *Anal*. Calcd. For $C_{20}H_{14}Cl_2N_4OS_2$ (461.38): C, 52.06, H, 3.06, N, 12.14%. Found: C, 52.19, H, 3.18, N, 12.03%.

References

1. H. R. Maradiya, *J. Saudi Chem. Soc*. 14 (2010) 77-81.
2. A Rao, A. Carbone, A. Chimirri, E. De Clercq, A. Monforte, P. Monforte, C. Pannecouque, M. Zappal, *Farmaco*. 58 (2003) 115-120.
3. M. E. Khalifa, Sh. H. Abdel-Hafez, A. A. Gobouri, and M. I. Kobeasy, *Phosphorus, Sulfur, and Silicon*, 190 (2015**)** 461-476.
4. T. Mosolygó, A. Kincses, A. Csonka, Á. S. Tönki, K. Witek, C. Sanmartín, et al., *Molecules*, (2019) 24-1487.
5. M. H. Abdellattif, A. A. H. Abdel-Rahman, M. M. H. Arief, S. M. Mouneir, A. Ali, M. A. Hussien, R. M. Okasha, T.H. Afifi and M. Hagar, *Front. Chem.* 9 (2021) 672503.
6. G. Spengler, A. Kincses, T. Mosolygó, M. A. Marć, M. Nové,M. Gajdács and E. Domínguez-Álvarez, *Molecules*, 24 (2019) 4264.
7. M. Casaril, M. Domingues, S. R. Bampi, D. de Andrade Lourenço, N. B. Padilha, E. J. Lenardão and L. Savegnago, *Psychopharmacology*, 236 (2019) 2867-2880.
8. N. Z. Alias, N. I. Hassan, Z. A. I. N. I. Yusoff, S. H. A. R. I. Z. A. L. Hasan and Ahmad, W. Y. W. Synthesis, *Sains Malaysiana*,. 47(2018) 347-352.
9. E. Shaban, S. H. Nassar, S. Shabban and H. E. Gaffer, *Egypt. J. Chem*. The 8th. Int. Conf. Text. Res. Div., Nat. Res. Centre, Cairo (2017) 73-78.
10. A. Amer, A. A. Abdelhamid, *J. Heterocycl. Chem*., 54 (2017) 3126-3132.
11. A. Amer, A. H. Moustafa, *Mol. Divers*, 21 (2017) 875-880.
12. A .F. Khlebnikov, M. S. Novikov, A. A. Amer, *Russian chemical bulletin*, 5 (2004) 1092-1101.12.
13. A. Amer, *J. Heterocyclic Chem.*, 55 (2018) 297.
14. H. Abdel-Ghany, A. M El-Sayed, A. A. Amer, A. M Ahmed, *J. Heterocycl. Chem*., 53(2016) 2013-2019
15. A. Amer, *Phosphorus, Sulfur, Silicon and the Related Elements*, 183 (2008) 2330–2343.
16. V. D. Dyachenko, Yu. A. Sharanin, V. P. Litvinov, V. N. Nesterov, V. E. Shklover, Yu. T. Struchkov V. K.Promonenkov and A. V. Turov, *Zh. Obshch. Khim*, 61 (199) 74.