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SYNTHESIS OF 1,4,6-TRISUBSTITUTED 2[1*H*]-PYRIMIDINE-SELENONES

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Abstract – 1,6-Diaryl-4-methyl-2[1*H*]-pyrimidineselenones and 1,4-diaryl-6-methyl-2[1*H*]-pyrimidineselenones were synthesised by treatment of appropriate pyrimidinethiones with gaseous H_2Se. 2D NMR spectroscopic studies were conducted to obtain conformations of the newly synthesised derivatives

INTRODUCTION

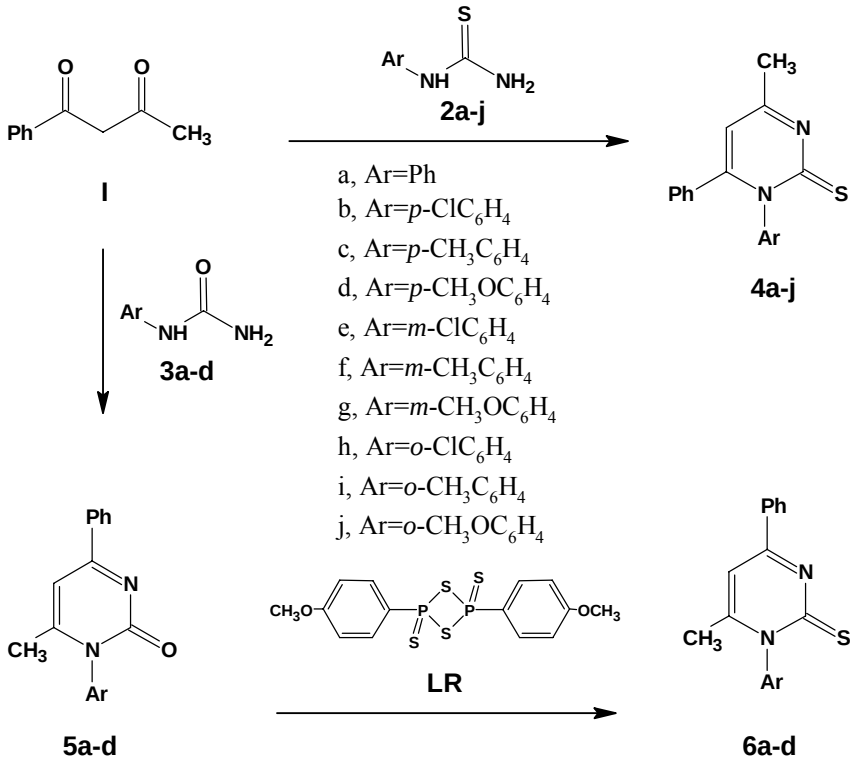
In the 1980's Katoh *et al.*[1] have studied reactivity and ways of the synthesis of the various 2[1*H*]-pyrimidinone and thione derivatives. Also they have reported antiinflammatory activity of these compounds.[2] Furthermore they corroborated selective synthesis of 1,4-diaryl-6-methyl- and 1,6-diaryl-4-methyl-2[1*H*]-pyrimidinones. Condensation of the benzoyloacetone derivatives with *N*-phenylurea gave 1,4-diaryl-6-methyl-2[1*H*]-pyrimidinones while the same reaction with *N*-phenylthiourea yielded 1,6-diaryl-4-methyl-2-[1*H*]-pyrimidinethiones, which were converted into the corresponding pyrimidinones.
In our earlier works we have focused on introduction of exocyclic atom of selenium into the five-membered heterocyclic rings of various derivatives of imidazolidine and thiazoline.[3-6] Introduction of selenium into the six-membered heterocyclic ring of pirymidine was investigated only for 1-aryl-4,6-dimethyl-2[1*H*]-pyrimidinethiones.[7] The general procedure to obtain the selenium derivatives was the treatment of quaternary heterocyclic ammonium salt with HSe^- ion. Recently it has been shown that for various derivatives of rhodanine this method hasn't been successful.[8,9] However the reaction of thiazolinium salts with gaseous H_2Se gave selenorhodanines with good yields.

The aim of the present work was to obtain various unsymetrically substituted derivatives of 2[1*H*]-pyrimidinethione and to check the possibility of the introduction of selenium atom to these compounds by previously described method.

RESULTS AND DISCUSSION

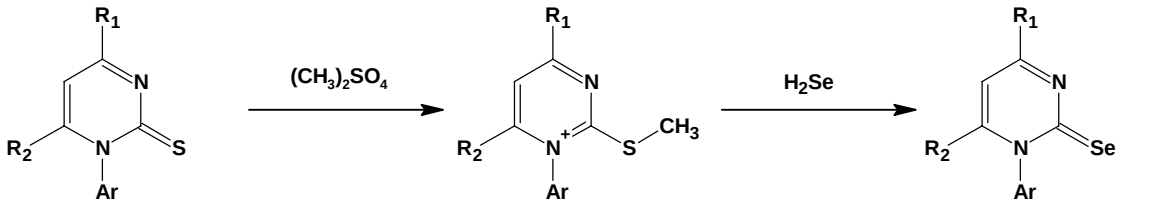
Synthesis

The first stage of the synthesis was to obtain unsymetrically 1,4,6-trisubstituted 2[1*H*]-pyrimidinethiones as a starting compounds for selenation reaction (Scheme 1). 1-Aryl-4-methyl-6-phenyl-2[1*H*]-



Scheme 1

pyrimidinethiones (**4a-j**) were prepared by condensation of benzoylacetone (**1**) and appropriate *N*-arylthioureas (**2a-j**) in the presence of conc. HCl in boiling ethanol. 1-Aryl-6-methyl-4-phenyl-2[1*H*]-pyrimidinethiones were obtained by two-step synthesis. Firstly, condensation of benzoylacetone and *N*-arylureas (**3a-d**) in acidic media gave 1-aryl-6-methyl-4-phenyl-2[1*H*]-pyrimidinones (**5a-d**). These precursors were treated with 2,4-bis(*p*-methoxyphenyl)-1,3,2,4-dithiadiphosphetane-2,4-disulfide (Lawesson's reagent, **LR**[10,11]) in boiling *m*-xylene to obtain the corresponding 1-aryl-6-methyl-4-phenyl-2-[1*H*]-pirymidinethiones (**6a-d**). The structure of the synthesized compounds was confirmed by NMR spectroscopy. Compounds (**4a-j**) and (**6a-d**) were the substrates for selenation reaction. These compounds were methylated by heating under nitrogen in boiling cyclohexanol bath for 45 min with an excess of dimethyl sulfate yielding pyrimidinium salts with thiomethyl group at the C-2 position. These salts were



4a-j R_1=CH_3, R_2=Ph
6a-d R_1=Ph, R_2=CH_3

7a-j R_1=CH_3, R_2=Ph
8a-d R_1=Ph, R_2=CH_3

Scheme 2

then treated with gaseous H_2Se in basic media for 1.5 hour at room temperature yielding appropriate 1,4,6-trisubstituted 2[1*H*]-pyrimidineselenones (**7a-j**, **8a-d**) (Scheme 2). Yields of obtained products are collected in Table 1.

Table 1. Yields of the 1,4,6-trisubstituted 2[1*H*]-pyrimidineselenones.

Compound	Yield %	Compound	Yield %
7a	39.3	**7h**	17.9
7b	36.1	**7i**	25.9
7c	39.8	**7j**	26.0
7d	34.7	**8a**	51.3
7e	50.5	**8b**	61.9
7f	19.0	**8c**	62.0
7g	29.5	**8d**	46.1

NMR spectral data

All the synthesized compounds were investigated by NMR spectroscopy to check the influence of selenium-sulphur exchange on NMR spectra. There were no significant changes observed in ^{13}C NMR spectra after comparison of pyrimidineselenones and appropriate pyrimidinethiones. In ^{1}H NMR spectra there is only one signal in pyrimidineselenones' spectra which is significantly shifted downfield – it is the signal of the vinyl proton in the pyrimidine ring. Moreover this difference is constant for all derivatives and yields 0.15 ppm. Chemical shifts for vinyl proton of investigated compounds are shown in Table 2. The rest of the spectra remains almost unchanged. These changes in chemical shift can be explained by the difference in electronegativity of sulfur and selenium in connection to electronic properties of α,β-unsaturated carbonyl systems. It is known, that for such structures, there is a second mesomeric form, with positive charge on β-atom, which induces increase of electron density on α- and γ-atom and in consequence shifts the NMR signal of protons connected to these atoms upfield. It seems that similar situation can occur in pyrimidine ring of investigated compounds, in which the vinyl proton of pyrimidine ring can be consider as a proton in position γ of unsaturated carbonyl system. Lower, in

Table 2. Chemical shifts of the vinyl proton in different derivatives of the 1,4,6-trisubstituted 2[1*H*]-pyrimidinethiones and selenones.

2[1*H*]-pyrimidinethione		2[1*H*]-pyrimidineselenone	
Compound	chemical shift δ	Compound	chemical shift δ
4a	6,58	**7a**	6,73
4b	6,58	**7b**	6,73
4c	6,56	**7c**	6,72
4d	6,56	**7d**	6,72
4e	6,57	**7e**	6,72
4f	6,56	**7f**	6,72
4g	6,56	**7g**	6,71
4h	6,57	**7h**	6,72
4i	6,57	**7i**	6,72
4j	6,53	**7j**	6,68
6a	7,09	**8a**	7,25
6b	7,09	**8b**	7,25
6c	7,07	**8c**	7,23
6d	7,07	**8d**	7,22

compare to sulfur, electronegativity of selenium diminish this effect and therefore can cause observed downfield shift of vinyl proton. Moreover, for pyrimidinones, NMR signal of the vinyl proton is shifted upfield due to higher electronegativity of oxygen (data not shown).

The comparison between ^{1}H NMR spectra of 1,4- and 1,6-diaryl derivatives showed some differences. The main is in the aromatic region. 1,4-Diaryl derivatives show so called "benzoyl pattern" for benzene ring which is the substitutent at the position 4 of pyrimidine moiety, that is protons in position *orto* of this ring are strongly deshielded and show up as a doublet or a multiplet at 8.2 ppm which was described previously for such derivatives.[1] Furthermore the vinyl proton signal of the 1,4-diaryl derivatives is shifted downfield by 0.5 ppm for all compounds in comparison to 1,6-diaryl derivatives (see Table 2). Such changes in the spectra can not be explained only in terms of changing chemical neighbourhood by position exchanging between the phenyl and methyl group, but differences in the conformations of these isomers should be considered. To evaluate the conformations of the investigated compounds the 2D NOESY experiment was used.[12] This experiment was conducted for all obtained 2[1*H*]-pyrimidineselenones. Significant NOE signals are indicated in Figure 1 for both isomers. Interaction between phenyl protons H_c and vinyl proton H_a in 1,4-diaryl derivatives is possible only if the benzene ring is coplanar with the pyrimidine ring. On the contrary the lack of such interactions between protons of

the second aryl substituent and methyl group indicates that the plane of this aryl moiety is strongly twisted against the plane of pyrimidine ring and can be even perpendicular to it. A similar situation occurs in the case of 1,6-diaryl derivatives where there is no interactions between aromatic protons of two aryl

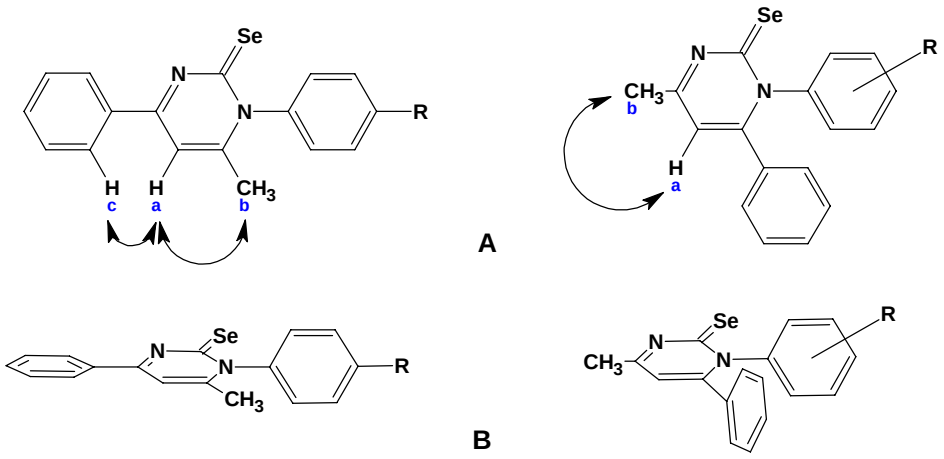


Figure 1. A – significant NOE interactions in 1,4-diaryl and 1,6-diaryl-2[1*H*]-pyrimidineselenones. B – proposed conformations.

substituents, and between aromatic protons of phenyl ring in position 6 and vinyl proton H_a. This result indicates that both aromatic rings in 1,6-diaryl isomers are twisted against the plane of the pyrimidine ring.

IR and UV spectra

The IR spectra of all investigated compounds are very similar. The only differences are observed in the positions of the absorption bands in the range corresponding to stretching vibrations of C=S or C=Se group. Compounds (**4a-j**) show $\nu_{C=S}$ band within the range 1267-1250 cm^{-1}, whereas 1,4-diaryl isomers (**6a-d**) within the range 1280-1277 cm^{-1}. Introduction of selenium shifts this band approximately 10 cm^{-1} towards lower wavenumbers. Much more significant are the differences between the positions of the bands in the range 943-830 cm^{-1}. There is a band within the range 943-862 cm^{-1} appearing in the spectra of thiones, whereas in the spectra of selenones this band is moved by 30 cm^{-1} towards lower wavenumbers.

The UV spectra of compounds (**4a-j**) show two absorption bands – at 300 and 385 nm. Introduction of selenium into these compounds cause a batochromic shift of the first band, which for selenones (**7a-j**) occurs at 335 nm and has no influence on the second one. Compounds (**6a-d**) show only one absorption band in UV spectra at 295 nm, which remains unchanged for selenium containing isologs (**8a-d**). The only difference between the UV spectra of **6a-d** and **8a-d** is the presence of the second absorption band, which occurs as a shoulder at 330 nm in the spectra of selenones.

Mass spectra

Both isomers (**7**) and (**8**) show very similar fragmentation pathways. For all investigated compounds the

molecular ion is simultaneously the base one. Rest of the signals is much less intense. Among them the most characteristic are signals of $[M - CH_3]^+$, $[M - Se]^+$, $[M - Se - Ar]^+$, and $[M - NCSe]^+$. Further there are characteristic signals of fragmentation of the phenyl moiety. These are the signals corresponding to fragments $C_7H_7^+$ (m/z=91), $C_6H_5^+$ (m/z=77), $C_5H_5^+$ (m/z=65) and $C_4H_3^+$ (m/z=51). Similar fragmentation pathway is observed for appropriate pyrimidinethiones.

EXPERIMENTAL

Meltings points (uncorrected) were determined on a Boetius apparatus. The UV spectra were measured with a Jenway 6505 UV/VIS spectrophotometer in chloroform. The IR spectra were recorded with Jasco FT IR – 670 Plus spectrophotometer in KBr discs. The NMR spectra were acquired in $CDCl_3$ using Varian Mercury-VX 300 MHz spectrometer. The EI MS spectra at 70 eV were taken with a Finnigan MAT 95S instrument. Elementary analyses were carried out with a Perkin Elmer 2400 instrument.

1-Aryl-4-methyl-6-phenyl-2[1H]-pyrimidinethiones (**4a-j**)

General procedure

The mixture of 1.62 g of benzoylacetone (**1**) (10 mmol) and appropriate thiourea (**2a-j**) (10 mmol) in the presence of 3.5 mL of conc. HCl in 30 mL of ethanol was refluxed for 6 h. Then the whole was neutralised with 10% NaOH and extracted with dichloromethane. The crude product was purified by column chromatography on silica gel with chloroform/acetone (100:4 v/v) and used without further purification.

4-Methyl-1,6-diphenyl-2[1H]-pyrimidinethione (**4a**) Yield: 39.0%, mp 212-213°C, IR (cm^{-1}) 1610 (ν C=N), 1590 (ν C=C), 1265 (ν C=S); UV (nm) 300, 325, 385; MS m/z (%): 278 (70) M^+, 277 (100) M^+-H; ^{1}H NMR δ 7.32-7.03 (10H, m, Ar-H), 6.58 (1H, s, H_a), 2.51 (3H, s, CH_3), ^{13}C NMR δ 185 (C=S), 170 (C-4), 159 (C-6), 141, 133, 130, 129, 128.9, 128.8, 128.6, 128.4 (C_{Ar}), 111.7 (C-5), 25 (CH_3); Anal. Calcd for $C_{17}H_{14}N_2S$: C, 73.35; H, 5.1; N, 10.1. Found: C, 73.4; H, 5.1; N, 9.9.

1-(p-Chlorophenyl)-4-methyl-6-phenyl-2[1H]-pyrimidinethione (**4b**) Yield: 34.3%, mp 209-211°C, IR (cm^{-1}) 1611 (ν C=N), 1593 (ν C=C), 1267 (ν C=S); UV (nm) 300, 385; MS m/z (%): 312 (78) M^+, 311 (100) M^+-H; ^{1}H NMR δ 7.35-7.19 (5H, m, Ar-H), 7.09-7.01 (4H, m, Ar-H), 6.58 (1H, s, H_a), 2.51 (3H, s, CH_3); ^{13}C NMR δ 185 (C=S), 170 (C-4), 159 (C-6), 140, 134, 133, 130, 129.8, 128.7, 128.5 (C_{Ar}), 111.7 (C-5), 25.5 (CH_3); Anal. Calcd for $C_{17}H_{13}N_2ClS$: C, 65.3; H, 4.2; N, 9.0. Found: C, 65.3; H, 4.2; N, 8.8.

4-Methyl-6-phenyl-1-(p-tolyl)-2[1H]-pyrimidinethione (**4c**) Yield: 36.4%, mp 203-205°C, IR (cm^{-1}) 1608 (ν C=N), 1590 (ν C=C), 1267 (ν C=S); UV (nm) 300, 325, 385; MS m/z (%): 292 (74.8) M^+, 291 (100) M^+-H; ^{1}H NMR δ 7.27-7.14 (3H, m, Ar-H), 7.08-7.02 (4H, m, Ar-H), 6.98-6.92 (2H, m, Ar-H), 6.56 (1H, s, H_a), 2.48 (3H, s, CH_3); 2.24 (3H, s, Ar-CH_3); ^{13}C NMR δ 185 (C=S), 169.8 (C-4), 159.6 (C-6), 139,

138.9, 133.5, 130, 129.9, 128.6, 128.4 (C_{Ar}), 111.7 (C-5), 25.5 (CH_3), 21.4 (Ar-CH_3); Anal. Calcd for $C_{18}H_{16}N_2S$: C, 73.9; H, 5.5; N, 9.6. Found: C, 73.9; H, 5.6; N, 9.5.

1-(p-Methoxyphenyl)-4-methyl-6-phenyl-2[1H]-pyrimidinethione (**4d**) Yield: 9.9%, mp 199-201°C, IR (cm^{-1}) 1613 (ν C=N), 1591 (ν C=C), 1251 (ν C=S); UV (nm) 300, 325, 335, 360, 385; MS m/z (%): 308 (92) M, 307 (100) M^+-H; ^{1}H NMR δ 7.29-7.16 (3H, m, Ar-H-3',4'), 7.10-7.03 (2H, m, Ar-H-2'), 7.02-6.95 (2H, m, Ar-H-3), 6.80-6.73 (2H, m, Ar-H-2), 6.56 (1H, s, H_a), 3.73 (3H, s, OCH_3), 2.50 (3H, s, CH_3); ^{13}C NMR δ 185.7 (C=S), 169.8 (C-4), 159.8 (C-6), 159.5 (C_{Ar}-4), 134.4, 133.7, 129.9, 129.8, 128.6, 128.5, 114.6 (C_{Ar}), 111.6 (C-5), 55.5 (OCH_3), 25.4 (CH_3); Anal. Calcd for $C_{18}H_{16}N_2OS$: C, 70.1; H, 5.2; N, 9.1. Found: C, 70.0; H, 5.3; N, 8.9.

1-(m-Chlorophenyl)-4-methyl-6-phenyl-2[1H]-pyrimidinethione (**4e**) Yield: 33.6%, mp 209-210°C, IR (cm^{-1}) 1613 (ν C=N), 1590 (ν C=C), 1267 (ν C=S); UV (nm) 300, 325, 385; MS m/z (%): 312 (74.8) M^+, 311 (100) M^+-H; ^{1}H NMR δ 7.31-6.95 (9H, m, Ar-H), 6.57 (1H, s, H_a), 2.50 (3H, s, CH_3); ^{13}C NMR δ 184.9 (C=S), 170.3 (C-4), 159.2 (C-6), 142.4, 135, 133, 130.4, 130.3, 129.2, 128.6, 127.4 (C_{Ar}), 111.7 (C-5), 25.5 (CH_3); Anal. Calcd for $C_{17}H_{13}N_2ClS$: C, 65.3; H, 4.2; N, 9.0. Found: C, 64.9; H, 4.1; N, 8.9.

4-Methyl-6-phenyl-1-(m-tolyl)-2[1H]-pyrimidinethione (**4f**) Yield: 29.7%, mp 168-170°C, IR (cm^{-1}) 1613 (ν C=N), 1589 (ν C=C), 1249 (ν C=S); UV (nm) 300, 325; MS m/z (%): 292 (69.8) M^+, 291 (100) M^+-H; ^{1}H NMR δ 7.28-6.85 (9H, m, Ar-H), 6.56 (1H, s, H_a), 2.50 (3H, s, CH_3), 2.22 (3H, s, Ar-CH_3); ^{13}C NMR δ 185.2 (C=S), 169.8 (C-4), 159.5 (C-6), 141.4, 139.5, 133.5, 129.9, 129.2, 128.5, 128.3, 125.8 (C_{Ar}), 111.6 (C-5), 25.4 (CH_3), 21.4 (Ar-CH_3); Anal. Calcd for $C_{18}H_{16}N_2S$: C, 73.9; H, 5.5; N, 9.6. Found: C, 73.8; H, 5.5; N, 9.8.

1-(m-Methoxyphenyl)-4-methyl-6-phenyl-2[1H]-pyrimidinethione (**4g**) Yield: 18.7%, mp 188-191°C, IR (cm^{-1}) 1606 (ν C=N), 1590 (ν C=C), 1256 (ν C=S); UV (nm) 300, 385; MS m/z (%): 308 (78) M, 307 (100) M^+-H; ^{1}H NMR δ 7.30-7.06 (6H, m, Ar-H), 6.78-6.65 (2H, m, Ar-H), 6.62 (1H, t, *J=2.2 Hz*, Ar-H-2), 6.56 (1H, s, H_a), 3.66 (3H, s, OCH_3), 2.50 (3H, s, CH_3); ^{13}C NMR δ 185 (C=S), 169.9 (C-4), 160.4 (C-6), 159.4 (C_{Ar}-4), 142.3, 133.4, 130.1, 130, 128.5, 121.2, 114.8 (C_{Ar}), 111.6 (C-5), 55.7 (OCH_3), 25.4 (CH_3); Anal. Calcd for $C_{18}H_{16}N_2OS$: C, 70.1; H, 5.2; N, 9.1. Found: C, 69.5; H, 5.3; N, 9.5.

1-(o-Chlorophenyl)-4-methyl-6-phenyl-2[1H]-pyrimidinethione (**4h**) Yield: 39.6%, mp 215-217°C, IR (cm^{-1}) 1616 (ν C=N), 1594 (ν C=C), 1267 (ν C=S); UV (nm) 300, 325, 385; MS m/z (%): 312 (10) M^+, 277 (100) M^+-Cl; ^{1}H NMR δ 7.34-7.14 (9H, m, Ar-H), 6.57 (1H, s, H_a), 2.52 (3H, s, CH_3); ^{13}C NMR δ 184.2 (C=S), 170.6 (C-4), 159.5 (C-6), 139.1, 132.8, 132, 130.9, 130.7, 130.4, 128.4, 127.8 (C_{Ar}), 111.5 (C-5), 25.6 (CH_3); Anal. Calcd for $C_{17}H_{13}N_2ClS$: C, 65.3; H, 4.2; N, 9.0. Found: C, 64.2; H, 4.1; N, 8.7.

4-Methyl-6-phenyl-1-(o-tolyl)-2[1H]-pyrimidinethione (**4i**) Yield: 41.5%, mp 216-219°C, IR (cm^{-1}) 1616 (ν C=N), 1594 (ν C=C), 1267 (ν C=S); UV (nm) 300, 385; MS m/z (%): 292 (75.7) M^+, 259 (100) M^+-

SH; ^{1}H NMR δ 7.30-7.00 (9H, m, Ar-H), 6.57 (1H, s, H_a), 2.52 (3H, s, CH_3), 2.11 (3H, s, Ar-CH_3); ^{13}C NMR δ 184.3 (C=S), 170.1 (C-4), 159.5 (C-6), 140.5, 134.8, 133.1, 131.5, 130.2, 129.4, 129, 127.1 (C_{Ar}), 111.6 (C-5), 25.5 (CH_3), 18.1 (Ar-CH_3); Anal. Calcd for $C_{18}H_{16}N_2S$: C, 73.9; H, 5.5; N, 9.6. Found: C, 73.4; H, 5.4; N, 9.6.

1-(o-Methoxyphenyl)-4-methyl-6-phenyl-2[1H]-pyrimidinethione (**4j**) Yield: 57.1%, mp 204-207°C, IR (cm^{-1}) 1609 (ν C=N), 1592 (ν C=C), 1266 (ν C=S); UV (nm) 300, 325, 385; MS m/z (%): 308 (12.1) M^+, 277 (100) M^+-OCH_3; ^{1}H NMR δ 7.26-7.02 (7H, m, Ar-H), 6.80 (1H, td, *J_3=7.4 Hz, J_4=1.1 Hz*, Ar-H-5), 6.75 (1H, dd, *J_3=8.25 Hz*, *J_4=1.1 Hz*, Ar-H-3), 6.53 (1H, s, H_a), 3.68 (3H, s, OCH_3), 2.48 (3H, s, CH_3); ^{13}C NMR δ 185 (C=S), 170 (C-4), 160.3 (C-6), 153.8 (C_{Ar}-4), 133.5, 130.7, 130, 129.7, 128.1, 121, 112.6 (C_{Ar}), 111.3 (C-5), 56 (OCH_3), 25.5 (CH_3); Anal. Calcd for $C_{18}H_{16}N_2OS$: C, 70.1; H, 5.2; N, 9.1. Found: C, 69.3; H, 5.3; N, 9.0.

1-Aryl-6-methyl-4-phenyl -2[1H]-pyrmidinones (**5a-d**)

General procedure

The mixture of 1.62 g of benzoylacetone (**1**) (10 mmol) and appropriate urea (**3a-d**) (10 mmol) in the presence of 4 mL of conc. HCl in 30 mL of ethanol was refluxed for 20-30 h. Then the mixture was neutralised with 10% NaOH and extracted with dichloromethane. The crude product was purified by column chromatography on silica gel with chloroform/acetone (100:4 v/v) and used for further reaction with Lawesson's reagent.

1-Aryl-6-methyl-4-phenyl -2[1H]-pyrmidinethiones (**6a-d**)

General procedure

The solution of 2[1*H*]-pyrimidinone (**5a-d**) (10 mmol) and 2.02 g of Lawesson's reagent (**LR**) (5 mmol) in 50 mL of *m*-xylene was refluxed for 1.5 h. After cooling, yellow precipitate was filtered off and purified by column chromatography on silica gel with chloroform/acetone (100:4 v/v) and used without further purification.

6-Methyl-1,4-diphenyl-2[1H]-pyrimidinethione (**6a**) Yield: 56.0%, mp 209-211°C, IR (cm^{-1}) 1605 (ν C=N), 1593 (ν C=C), 1281 (ν C=S); UV (nm) 295; MS m/z (%): 278 (74.5) M^+, 277 (100) M^+-H; ^{1}H NMR δ 8.21-8.15 (2H, m, Ar-H-2'), 7.60-7.40 (6H, m, Ar-H), 7.26-7.20 (2H, m, Ar-H-2), 7.10 (1H, s, H_a), 2.10 (3H, d, *J=0.55 Hz*, CH_3), ^{13}C NMR δ 185.2 (C=S), 164.5 (C-4), 158.8 (C-6), 141.8, 135.3, 132.6, 130.6, 129.6, 129, 128.6, 127.1 (C_{Ar}), 107.2 (C-5), 23.2 (CH_3); Anal. Calcd for $C_{17}H_{14}N_2S$: C, 73.35; H, 5.1; N, 10.1. Found: C, 73.1; H, 5.0; N, 10.0.

1-(p-Chlorophenyl)-6-methyl-4-phenyl-2[1H]-pyrimidinethione (**6b**) Yield: 62.0%, mp 232-234°C, IR (cm^{-1}) 1600 (ν C=N), 1580 (ν C=C), 1281 (ν C=S); UV (nm) 295; MS m/z (%): 312 (81.5) M^+, 311 (100) M^+-H; ^{1}H NMR δ 8.20-8.15 (2H, m, Ar-H-2'), 7.60-7.40 (5H, m, Ar-H), 7.23-7.17 (2H, m, Ar-H-2), 7.10

(1H, s, H_a), 2.14 (3H, d, *J=0.55 Hz*, CH_3), ^{13}C NMR δ 185.2 (C=S), 164.7 (C-4), 158.4 (C-6), 140.1, 135.6, 135.1, 132.8, 131, 129.1, 128.7, 128.6 (C_{Ar}), 107.2 (C-5), 23.2 (CH_3); Anal. Calcd for $C_{17}H_{13}N_2ClS$: C, 65.3; H, 4.2; N, 9.0. Found: C, 65.3; H, 4.2; N, 9.0.

6-Methyl-4-phenyl-1-(p-tolyl)-2[1H]-pyrimidinethione (**6c**) Yield: 74.7%, mp 212-215°C, IR (cm^{-1}) 1601 (ν C=N), 1591 (ν C=C), 1275 (ν C=S); UV (nm) 295; MS m/z (%): 292 (79.1) M^+, 291 (100) M^+-H; ^{1}H NMR δ 8.20-8.14 (2H, m, Ar-H-2'), 7.58-7.30 (5H, m, Ar-H), 7.13-7.09 (2H, m, Ar-H-2), 7.07 (1H, s, H_a), 2.42 (3H, s, Ar-CH_3), 2.12 (3H, s, CH_3), ^{13}C NMR δ 185.4 (C=S), 164.3 (C-4), 159 (C-6), 139.7, 139.3, 135.3, 132.5, 131.3, 129, 128.6, 126.8 (C_{Ar}), 107.2 (C-5), 23.2 (CH_3), 21.6 (Ar-CH_3); Anal. Calcd for $C_{18}H_{16}N_2S$: C, 73.9; H, 5.5; N, 9.6. Found: C, 73.3; H, 5.4; N, 9.5.

1-(p-Methoxyphenyl)-6-methyl-4-phenyl-2[1H]-pyrimidinethione (**6d**) Yield: 74.7%, mp 226-229°C, IR (cm^{-1}) 1603 (ν C=N), 1596 (ν C=C), 1247 (ν C=S); UV (nm) 295; MS m/z (%): 308 (100) M^+; ^{1}H NMR δ 8.20-8.15 (2H, m, Ar-H-2'), 7.58-7.44 (3H, m, Ar-H), 7.17-7.00 (5H, m, Ar-H-2, H_a), 3.86 (3H, s, OCH_3), 2.14 (3H, d, *J=0.55 Hz*, CH_3), ^{13}C NMR δ 185.7 (C=S), 164.3 (C-4), 160.1 (C-6), 159.3 (C_{Ar}-4), 135.3, 134.6, 132.5, 129, 128.6, 115.8 (C_{Ar}), 107.2 (C-5), 55.7 (OCH_3), 23.2 (CH_3); Anal. Calcd for $C_{18}H_{16}N_2OS$: C, 70.1; H, 5.2; N, 9.1. Found: C, 69.6; H, 5.2; N, 9.0.

1,4,6-Trisubstituted 2[1H]-pyrimidineselenones (**7a-j**, **8a-d**).

General procedure

The mixture of appropriate 2[1*H*]-pyrimidinethione (**4a-j**, **6a-d**) (1.5 mmol) and 189-756 mg of dimethyl sulfate (1.5-6 mmol) was heated in boiling cyclohexanol bath for 45 min under nitrogen atmosphere. The obtained syrup was dissolved in abs. ethanol (15 mL) and alkalised with piperidine (5 mL). The mixture was treated with H_2Se, obtained from 13.5 g of FeSe (0.1 mol) and 25 % HCl (200 mL), under nitrogen atmosphere for 90 min at rt. Nitrogen was purged for another 2 h to remove the excess of H_2Se, which was absorbed in Pb(II) salt solution. The reaction mixture was then evaporated under reduced pressure and separated by column chromatography on silica gel with chloroform/acetone (100:4 v/v). After solvent evaporation pure, homogeneous product was obtained with moderate yield.

4-Methyl-1,6-diphenyl-2[1H]-pyrimidineselenone (**7a**) Yield: 39.3%, mp 215-217°C, IR (cm^{-1}) 1606 (ν C=N), 1589 (ν C=C), 1255 (ν C=Se); UV (nm) 335, 360; MS m/z (%): 325 (82) M^+, 326 (100) M^++1; ^{1}H NMR δ 7.34-7.03 (10H, m, Ar-H), 6.73 (1H, s, H_a), 2.50 (3H, s, CH_3), ^{13}C NMR δ 186.2 (C=Se), 168.7 (C-4), 159.8 (C-6), 143, 133.3, 130.1, 129.8, 129.5, 129.2, 128.9, 128.4 (C_{Ar}), 113.6 (C-5), 25.5 (CH_3); Anal. Calcd for $C_{17}H_{14}N_2Se$: C, 62.8; H, 4.3; N, 8.6. Found: C, 62.9; H, 4.4; N, 8.5.

1-(p-Chlorophenyl)-4-methyl-6-phenyl-2[1H]-pyrimidineselenone (**7b**) Yield: 36.1%, mp 213-215°C, IR (cm^{-1}) 1613 (ν C=N), 1593 (ν C=C), 1261 (ν C=Se); UV (nm) 330, 370, 385; MS m/z (%): 359 (77,9) M^+, 360 (100) M^++1; ^{1}H NMR δ 7.34-7.20 (5H, m, Ar-H), 7.12-7.03 (4H, m, Ar-H), 6.73 (1H, s, H_a), 2.49

(3H, s, CH_3); ^{13}C NMR δ 186.2 (C=Se), 169 (C-4), 159.7 (C-6), 141.4, 135.1, 133, 130.4, 130.3, 129.9, 128.5 (C_{Ar}), 113.6 (C-5), 25.5 (CH_3); Anal. Calcd for $C_{17}H_{13}N_2ClSe$: C, 56.8; H, 3.6; N, 7.8. Found: C, 57.2; H, 3.7; N, 7.8.

4-Methyl-6-phenyl-1-(p-tolyl)-2[1H]-pyrimidineselenone (**7c**) Yield: 39.8%, mp 202-203°C, IR (cm^{-1}) 1609 (ν C=N), 1590 (ν C=C), 1259 (ν C=Se); UV (nm) 335, 385; MS m/z (%): 339 (83,4) M^+, 340 (100) M^++1; ^1H NMR δ 7.28-7.17 (3H, m, Ar-H), 7.12-6.98 (6H, m, Ar-H), 6.72 (1H, s, H_a), 2.49 (3H, d, *J=0.55 Hz*, CH_3); 2.26 (3H, s, Ar-CH_3); ^{13}C NMR δ 186 (C=Se), 169 (C-4), 160 (C-6), 141, 139, 133, 130.2, 130.1, 128.6, 128.4 (C_{Ar}), 113.7 (C-5), 25.5 (CH_3), 21.5 (Ar-CH_3); Anal. Calcd for $C_{18}H_{16}N_2Se$: C, 63.7; H, 4.75; N, 8.3. Found: C, 63.9; H, 4.8; N, 8.2.

1-(p-Methoxyphenyl)-4-methyl-6-phenyl-2[1H]-pyrimidineselenone (**7d**) Yield: 34.7%, mp 203-205°C, IR (cm^{-1}) 1614 (ν C=N), 1591 (ν C=C), 1251 (ν C=Se); UV (nm) 330, 385; MS m/z (%): 355 (59.8) M^+, 356 (100) M^++1; ^1H NMR δ 7.30-7.18 (3H, m, Ar-H-3',4'), 7.08-7.00 (4H, m, Ar-H-2, Ar-H-2'), 6.80 (2H, d, *J=8.8 Hz*, Ar-H-3), 6.72 (1H, s, H_a), 3.73 (3H, s, OCH_3), 2.49 (3H, s, CH_3); ^{13}C NMR δ 186.6 (C=Se), 168.6 (C-4), 160.3 (C-6), 159.7 (C_{Ar}-4), 135.9, 133.5, 130.1, 129.8, 128.6, 128.5, 114.7 (C_{Ar}), 113.6 (C-5), 55.5 (OCH_3), 25.5 (CH_3); Anal. Calcd for $C_{18}H_{16}N_2OSe$: C, 60.85; H, 4.5; N, 7.9. Found: C, 60.8; H, 4.5; N, 7.7.

1-(m-Chlorophenyl)-4-methyl-6-phenyl-2[1H]-pyrimidineselenone (**7e**) Yield: 50.5%, mp 204-206°C, IR (cm^{-1}) 1612 (ν C=N), 1587 (ν C=C), 1258 (ν C=Se); UV (nm) 330, 370, 385; MS m/z (%): 359 (79,2) M^+, 360 (100) M^++1; ^1H NMR δ 7.33-7.03 (9H, m, Ar-H), 6.72 (1H, s, H_a), 2.48 (3H, s, CH_3); ^{13}C NMR δ 186 (C=Se), 169 (C-4), 159.6 (C-6), 143.7, 135, 132.9, 130.4, 129.4, 128.7, 128.5, 127.4 (C_{Ar}), 113.6 (C-5), 25.6 (CH_3); Anal. Calcd for $C_{17}H_{13}N_2ClSe$: C, 56.8; H, 3.6; N, 7.8. Found: C, 56.8; H, 3.7; N, 7.8.

4-Methyl-6-phenyl-1-(m-tolyl)-2[1H]-pyrimidineselenone (**7f**) Yield: 19.0%, mp 185-187°C, IR (cm^{-1}) 1608 (ν C=N), 1587 (ν C=C), 1243 (ν C=Se); UV (nm) 335, 385; MS m/z (%): 339 (82,5) M^+, 340 (100) M^++1; ^1H NMR δ 7.29-7.02 (9H, m, Ar-H), 6.72 (1H, s, H_a), 2.49 (3H, s, CH_3), 2.22 (3H, s, Ar-CH_3); ^{13}C NMR δ 186 (C=Se), 168.6 (C-4), 159.9 (C-6), 142.8, 139.6, 133.3, 130.1, 129.9, 128.5, 128.4, 126 (C_{Ar}), 113.5 (C-5), 25.5 (CH_3), 21.4 (Ar-CH_3); Anal. Calcd for $C_{18}H_{16}N_2Se$: C, 63.7; H, 4.75; N, 8.3. Found: C, 63.9; H, 4.8; N, 8.2.

1-(m-Methoxyphenyl)-4-methyl-6-phenyl-2[1H]-pyrimidineselenone (**7g**) Yield: 29.5%, mp 193-196°C, IR (cm^{-1}) 1602 (ν C=N), 1587 (ν C=C), 1248 (ν C=Se); UV (nm) 335, 385; MS m/z (%): 355 (65) M^+, 356 (100) M^++1; ^1H NMR δ 7.31-7.15 (4H, m, Ar-H), 7.11-7.05 (2H, m, Ar-H-2'), 6.81-6.72 (2H, m, Ar-H-4,5), 6.72 (1H, s, H_a), 6.67 (1H, t, *J=1.9 Hz*, Ar-H-2), 3.68 (3H, s, OCH_3), 2.49 (3H, s, CH_3); ^{13}C NMR δ 185.9 (C=Se), 168.6 (C-4), 160.4 (C-6), 159.8 (C_{Ar}-4), 143.7, 133.3, 130.2, 128.5, 121.2, 114.9 (C_{Ar}),

113.5 (C-5), 55.7 (OCH_3), 25.4 (CH_3); Anal. Calcd for $C_{18}H_{16}N_2OSe$: C, 60.85; H, 4.5; N, 7.9. Found: C, 60.9; H, 4.5; N, 7.9.

1-(o-Chlorophenyl)-4-methyl-6-phenyl-2[1H]-pyrimidineselenone (**7h**) Yield: 17.9%, mp 208-210°C, IR (cm^{-1}) 1613 (ν C=N), 1591 (ν C=C), 1258 (ν C=Se); UV (nm) 335, 385; MS m/z (%): 359 (30) M^+, 360 (100) M^++1; ^{1}H NMR δ 7.35-7.14 (9H, m, Ar-H), 6.72 (1H, s, H_a), 2.50 (3H, s, CH_3); ^{13}C NMR δ 185.5 (C=Se), 169.2 (C-4), 160.1 (C-6), 140.3, 132.6, 131.8, 131.1, 130.8, 130.7, 128.4, 127.8 (C_{Ar}), 113.4 (C-5), 25.6 (CH_3); Anal. Calcd for $C_{17}H_{13}N_2ClSe$: C, 56.8; H, 3.6; N, 7.8. Found: C, 56.1; H, 3.6; N, 7.5.

4-Methyl-6-phenyl-1-(o-tolyl)-2[1H]-pyrimidineselenone (**7i**) Yield: 25.9%, mp 212-215°C, IR (cm^{-1}) 1612 (ν C=N), 1591 (ν C=C), 1258 (ν C=Se); UV (nm) 325; MS m/z (%): 339 (9.4) M^+, 259 (100) M^+-Se; ^{1}H NMR δ 7.31-7.05 (9H, m, Ar-H), 6.72 (1H, s, H_a), 2.50 (3H, s, CH_3), 2.11 (3H, s, Ar-CH_3); ^{13}C NMR δ 185.3 (C=Se), 168.8 (C-4), 160 (C-6), 141.7, 134.6, 132.9, 131.6, 130.4, 129.6, 129.2, 127.1 (C_{Ar}), 113.4 (C-5), 25.5 (CH_3), 18.4 (Ar-CH_3); Anal. Calcd for $C_{18}H_{16}N_2Se$: C, 63.7; H, 4.75; N, 8.3. Found: C, 63.7; H, 4.8; N, 8.2.

1-(o-Methoxyphenyl)-4-methyl-6-phenyl-2[1H]-pyrimidineselenone (**7j**) Yield: 26.0%, mp 193-196°C, IR (cm^{-1}) 1606 (ν C=N), 1590 (ν C=C), 1253 (ν C=Se); UV (nm) 330, 385; MS m/z (%): 355 (9.9) M^+, 325 (100) M^+-OCH_3; ^{1}H NMR δ 7.29-7.08 (7H, m, Ar-H), 6.86 (1H, t, J_3=*7.4 Hz*, Ar-H-5), 6.79 (1H, d, J_3=*8.5 Hz*, Ar-H-3), 6.68 (1H, s, H_a), 3.72 (3H, s, OCH_3), 2.48 (3H, s, CH_3); ^{13}C NMR δ 186 (C=Se), 168.7 (C-4), 160.7 (C-6), 153.7 (C_{Ar}-4), 133.3, 132, 131, 130.2, 128.1, 121.1, 112.7 (C_{Ar}), 113.2 (C-5), 56 (OCH_3), 25.5 (CH_3); Anal. Calcd for $C_{18}H_{16}N_2OSe$: C, 60.85; H, 4.5; N, 7.9. Found: C, 60.8; H, 4.6; N, 7.8.

6-Methyl-1,4-diphenyl-2[1H]-pyrimidineselenone (**8a**) Yield: 51.3%, mp 214-215°C, IR (cm^{-1}) 1601 (ν C=N), 1590 (ν C=C), 1272 (ν C=Se); UV (nm) 295, 330_{sh}; MS m/z (%): 325 (81.5) M^+, 326 (100) M^++1; ^{1}H NMR δ 8.23-8.18 (2H, m, Ar-H-2'), 7.63-7.45 (6H, m, Ar-H), 7.31-7.23 (3H, m, Ar-H-2, H_a), 2.18 (3H, s, CH_3), ^{13}C NMR δ 185.5 (C=Se), 163 (C-4), 159.2 (C-6), 143.2, 134.9, 132.8, 130.7, 129.8, 129.1, 128.8, 127.2 (C_{Ar}), 109 (C-5), 23.6 (CH_3); Anal. Calcd for $C_{17}H_{14}N_2Se$: C, 62.8; H, 4.3; N, 8.6. Found: C, 62.5; H, 4.3; N, 8.5.

1-(p-Chlorophenyl)-6-methyl-4-phenyl-2[1H]-pyrimidineselenone (**8b**) Yield: 61.9%, mp 236-238°C, IR (cm^{-1}) 1601 (ν C=N), 1596 (ν C=C), 1272 (ν C=Se); UV (nm) 300, 330_{sh}; MS m/z (%): 359 (77.1) M^+, 360 (100) M^++1; ^{1}H NMR δ 8.23-8.17 (2H, m, Ar-H-2'), 7.62-7.46 (5H, m, Ar-H), 7.28-7.22 (3H, m, Ar-H-2, H_a), 2.18 (3H, d, *J=0.55 Hz*, CH_3), ^{13}C NMR δ 185.5 (C=Se), 163.1 (C-4), 158.9 (C-6), 141.5, 135.9, 134.8, 133, 131.1, 129.2, 128.8, (C_{Ar}), 109.1 (C-5), 23.6 (CH_3); Anal. Calcd for $C_{17}H_{13}N_2ClSe$: C, 56.8; H, 3.6; N, 7.8. Found: C, 56.2; H, 3.7; N, 7.7.

6-Methyl-4-phenyl-1-(p-tolyl)-2[1H]-pyrimidineselenone (**8c**) Yield: 62.0%, mp 221-223°C, IR (cm^{-1}) 1600 (ν C=N), 1588 (ν C=C), 1267 (ν C=Se); UV (nm) 295, 330_{sh}; MS m/z (%): 339 (81.7) M^+, 340 (100) M^++1; ^{1}H NMR δ 8.23-8.17 (2H, d, *J=7 Hz*, Ar-H-2'), 7.58-7.45 (3H, m, Ar-H), 7.38 (2H, d, *J=8.5 Hz*, Ar-H-3), 7.23 (1H, s, H_a), 7.16 (2H, d, *J=8.5 Hz*, Ar-H-2), 2.43 (3H, s, Ar-CH_3), 2.18 (3H, s, CH_3), ^{13}C NMR δ 185.6 (C=Se), 162.8 (C-4), 159.4 (C-6), 140.7, 139.9, 135, 132.7, 131.3, 129.1, 128.7, 126.8 (C_{Ar}), 109 (C-5), 23.6 (CH_3), 21.6 (Ar-CH_3); Anal. Calcd for $C_{18}H_{16}N_2Se$: C, 63.7; H, 4.75; N, 8.3. Found: C, 63.6; H, 4.7; N, 8.3.

1-(p-Methoxyphenyl)-6-methyl-4-phenyl-2[1H]-pyrimidineselenone (**8d**) Yield: 46.1%, mp 218-220°C, IR (cm^{-1}) 1604 (ν C=N), 1593 (ν C=C), 1271 (ν C=Se); UV (nm) 295, 330_{sh}; MS m/z (%): 355 (57.9) M^+, 356 (100) M^++1; ^{1}H NMR δ 8.23-8.15 (2H, m, Ar-H-2'), 7.60-7.45 (3H, m, Ar-H), 7.22 (1H, s, H_a), 7.21 (2H, d, *J=9.1 Hz*, Ar-H-2), 7.19 (2H, d, *J=9.1 Hz*, Ar-H-3), 3.87 (3H, s, OCH_3), 2.19 (3H, d, *J=0.55 Hz*, CH_3), ^{13}C NMR δ 186 (C=Se), 162.7 (C-4), 160.3 (C-6), 159.7 (C_{Ar}-4), 136.1, 135, 132.7, 129.1, 128.8, 115.8 (C_{Ar}), 109 (C-5), 55.7 (OCH_3), 23.6 (CH_3); Anal. Calcd for $C_{18}H_{16}N_2OSe$: C, 60.85; H, 4.5; N, 7.9. Found: C, 60.8; H, 4.5; N, 7.7.

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