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Synthesis and characterization of pyrimidyl- and pyrazinylselenium compounds: X-ray structure of 2,5-bis(methylselenenyl)pyrazine

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ABSTRACT

A methodology for the lithiation of pyrimidine (**1a**) was developed and used for the synthesis of pyrimidylselenium compounds. The procedure involved prior complexation of **1a** with 2.2 equiv. of $BF_3{\cdot}Et_2O$ followed by a reaction with LDA or LTMP. The pyrazinylselenium derivatives were synthesized from the direct lithiation of pyrazine (**1b**) as the BF_3-directed lithiation failed to give the desired products. All the synthesized compounds were characterized by elemental analysis, NMR (^1H and ^{13}C) and Mass spectroscopy. In addition, 2,5-bis(methylselenenyl)pyrazine (**9b**) was characterized by single crystal X-ray crystallography.

1. Introduction

Organoseleniums with electron-deficient heterocycles have shown tremendous potential as biologically active agents [1–5], precursors to semi-conducting materials [6–8] and synthons in organic synthesis [9,10]. The chemistry of pyridylseleniums has grown substantially in the last couple of decades [11–15], and that of pyrimidylseleniums has recently shown some activity [11,16–21]. Surprisingly, there is no report on the chemistry of pyrazinylselenium compounds. We are reporting here the synthesis and characterization of pyrimidyl- and pyrazinylselenium compounds by a methodology that involves the lithiation of pyrimidine (**1a**) and pyrazine (**1b**), respectively. The direct lithiation of unsubstituted pyrimidine has always been a challenge due to the instability of the lithiated pyrimidine species [22], whereas that of **1b** has been achieved with moderate success [22,23]. Recently, the BF_3-directed metallation of substituted pyrimidines (2,4-dimethoxy-, 2-butoxypyrimidine, etc.) and pyrazines (2-chloro-, 2-bromopyrazine, etc.) has been reported with highly expensive bimetallic tetramethylpiperdine (TMP) bases, TMPZnCl·LiCl and $(TMP)_2Mg{\cdot}2LiCl$ [24]. However, there is no report on the BF_3-directed lithiation of **1a** and **1b** with lithium diisopropylamide (LDA) or lithium tetramethylpiperdide (LTMP). The present paper provides detailed investigation on the lithiation of **1a** and **1b** in the presence and absence of $BF_3{\cdot}Et_2O$ with LDA and LTMP as the lithiating reagents, and selenium as the electrophile.

2. Experimental

2.1. General

All the reagents and solvents were purified by standard procedures, and were freshly distilled prior to use [25]. LTMP and LDA were prepared by the reaction of *n*-BuLi with 2,2,6,6-tetramethylpiperidine and diisopropylamine, respectively [26]. All the experiments were carried out in flame-dried round bottom flasks and under moisture-free nitrogen atmosphere. ^1H and ^{13}C NMR spectra were obtained on a Bruker 400 MHz spectrophotometer in $CDCl_3$. ^1H NMR and ^{13}C NMR chemical shifts were cited with respect to tetramethylsilane as the internal standard. The EI mass spectra were measured using a Shimadzu GC-Mass Spectrometer equipped with an Rtx-1MS (30 m × 0.25 mm ID × 0.25 μm) capillary column. Elemental analysis for C, H and N was carried out on a Vario MICRO Elementar analyzer.

2.2. 2-(Methylselenenyl)pyrimidine (*4a*)

1a (0.72 g, 0.70 mL, 9.0 mmol) was treated with a solution of $BF_3.Et_2O$ in diethyl ether (2.81 g, 2.48 mL, 19.8 mmol) at 0 °C. The

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temperature of the resulting suspension was lowered to −78 °C and LDA/LTMP (18.0 mmol) was added via cannulation. The orange solution thus formed was stirred for 15 min at −78 °C and elemental selenium (1.41 g, 18.0 mmol) was added to it. The temperature of the reaction mixture was slowly raised to the room temperature and stirring was continued till most of the selenium was dissolved. The resulting solution was re-cooled to −78 °C and reacted with iodomethane (2.56 g, 1.11 mL, 18.0 mmol). The reaction mixture was slowly brought back to the room temperature and hydrolyzed with distilled water (30 mL). The organic layer was extracted with diethyl ether and dried over anhydrous sodium sulfate. The solvent was removed using a rota-evaporator and the crude product was purified with column chromatography (silica gel 60–120 mesh, hexane/EtOAc, 50:1) to give **4a** (1.09 g, 70%, LDA and 1.12 g, 71%, LTMP) as a brownish red viscous liquid. ^{1}H NMR: (400 MHz, $CDCl_3$): δ (ppm): 8.60–8.61 (d, J = 4.8 Hz, 2H), 7.23–7.25 (t, 1H), 2.40 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 169.0, 157.6, 117.7, 6.4. MS (EI, 70 eV) m/z (relative intensity): 174 (18, $[M]^+$, ^{80}Se) 94 (100), 80 (25), 67 (6), 53 (41). *Anal.* Calc. for $C_5H_6N_2Se$: C, 34.69, H, 3.49, N, 16.18. Found: C, 34.82, H, 3.39, N, 16.27%.

*2.2.1. 2-(Ethylselenenyl)pyrimidine (**5a**)*

1a (0.72 g, 0.70 mL, 9.0 mmol), LDA (18.0 mmol), selenium (1.41 g, 18.0 mmol) and iodoethane (2.81 g, 1.45 mL, 18.0 mmol) were used to obtain **5a** (1.08 g, 64%) as a red viscous liquid. ^{1}H NMR: (400 MHz, $CDCl_3$): δ (ppm): 8.58–8.59 (d, J = 4.8 Hz, 2H), 7.20–7.22 (t, 1H), 2.91–2.96 (q, 2H), 1.41–1.44 (t, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 168.8, 157.5, 117.4, 23.1, 15.0. MS (EI, 70 eV) m/z (relative intensity): 188 (22, $[M]^{\cdot+}$, ^{80}Se), 173 (4), 159 (4), 107 (100), 79 (31), 68 (4), 53 (22). *Anal.* Calc. for $C_6H_8N_2Se$: C, 38.29, H, 4.25, N, 14.89. Found: C, 38.01, H, 4.16, N, 14.96%.

*2.2.2. 2,4-Bis(methylselenenyl)pyrimidine (**6a**)*

1a (0.72 g, 0.70 mL, 9.0 mmol), LDA (19.8 mmol), selenium (1.56 g, 19.8 mmol) and iodomethane (2.80 g, 1.22 mL, 19.8 mmol) were used to get **6a** (0.50 g, 21%) as a red viscous liquid. ^{1}H NMR: (400 MHz, $CDCl_3$): δ (ppm): 7.94–7.96 (d, J = 5.2 Hz, 1H), 6.91–6.92 (d, J = 5.4 Hz, 1H), 2.39 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 168.2, 154.0, 117.8, 6.7, 5.2. MS (EI, 70 eV) m/z (relative intensity): 268 (77, $[M]^{\cdot+}$, ^{80}Se), 252 (2), 185 (18), 174 (29), 108 (27), 93 (100), 79 (31), 65 (2), 52 (30). *Anal.* Calc. for $C_6H_8N_2Se_2$: C, 27.08, H, 3.03, N, 10.52. Found: C, 27.19, H, 3.16, N, 10.41%.

*2.2.3. 2,4,6-Tris(methylselenenyl)pyrimidine (**7a**)*

1a (0.72 g, 0.70 mL, 9.0 mmol), LDA (29.7 mmol), selenium (2.34 g, 29.7 mmol) and iodomethane (4.21 g, 1.50 mL, 29.7 mmol) were used to obtain **7a** (0.16 g, 5%) as an orange viscous liquid. ^{1}H NMR: (400 MHz, $CDCl_3$): δ (ppm): 6.98 (s, 1H), 2.45 (s, 3H), 2.42 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 168.1, 154.1, 117.2, 6.7, 5.4. MS (EI, 70 eV) m/z (relative intensity): 360 (70, $[M]^{\cdot+}$, ^{80}Se), 343 (59), 327 (11), 281 (41), 267 (18), 251 (17), 207 (83), 193 (19), 173 (28), 147 (29), 118 (18), 95 (82), 85 (100), 73 (88), 57 (39). *Anal.* Calc. for $C_7H_{10}N_2Se_3$: C, 23.41, H, 2.80, N, 7.80. Found: C, 23.48, H, 2.89, N, 7.88%.

*2.3. General method for the preparation of selenolate anion of pyrazine (**1b**)*

A solution of **1b** (1 g, 12.5 mmol) in dry THF (30 mL) was cooled to –78 °C and LDA (13.75 mmol) was added slowly via cannulation. After 15 min of stirring, elemental selenium (1.08 g, 13.75 mmol) was added to it. The temperature was slowly raised till all of the selenium was dissolved. Different electrophiles (13.75 mmol) were added to the selenolate anion at –78 °C to give the desired products.

*2.3.1. 2-(Methylselenenyl)pyrazine (**4b**)*

Iodomethane (1.95 g, 0.85 mL, 13.75 mmol) was used as the electrophile in the above reaction to give **4b** (1.3 g, 64%) as a pale yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 8.55–8.56 (d, J = 1.5 Hz, 1H), 8.38–8.40 (dd, J = 1.7 and 2.4 Hz, 1H), 8.22–8.23 (d, J = 2.6 Hz, 1H), 2.47 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 154.1, 145.7, 144.8, 140.1, 5.3. MS (EI, 70 eV) m/z (relative intensity): 174 (25, $[M]^{\cdot+}$, ^{80}Se), 132 (7), 94 (100), 79 (17), 52 (49). *Anal.* Calc. for $C_5H_6N_2Se$: C, 34.69, H, 3.49, N, 16.18. Found: C, 34.77, H, 3.55, N, 16.07%.

*2.3.2. 2-(Propylselenenyl)pyrazine (**5b**)*

Iodopropane (2.3 g, 1.34 mL, 13.75 mmol) was used instead of iodomethane to give **5b** (1.30 g, 53%) as a pale yellow liquid. ^{1}H NMR: (400 MHz, $CDCl_3$): δ (ppm): 8.53–8.54 (d, J = 1.5 Hz, 1H), 8.37–8.38 (dd, J = 1.6 and 2.5 Hz, 1H), 8.21–8.22 (d, J = 2.6 Hz, 1H), 3.17–3.20 (t, 2H), 1.77–1.86 (m, 2H), 1.02–1.06 (t, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 154.1, 146.4, 144.9, 140.2, 23.9, 23.5, 14.4. MS (EI, 70 eV) m/z (relative intensity): 204 (6, $[M]^{\cdot+}$, ^{80}Se), 202 (32), 160 (90), 121 (100), 107 (24), 94 (12), 79 (63), 68 (26), 52 (83). *Anal.* Calc. for $C_7H_{10}N_2Se$: C, 41.80, H, 5.01, N, 13.92. Found: C, 42.03, H, 5.18, N, 13.81%.

*2.3.3. 2-(Butylselenenyl)pyrazine (**6b**)*

Iodobutane (2.53 g, 1.56 mL, 13.75 mmol) was used as the electrophile to give **6b** (1.37 g, 51%) as a pale yellow liquid. ^{1}H NMR: (400 MHz, $CDCl_3$): δ (ppm): 8.53–8.54 (d, J = 1.5 Hz, 1H), 8.37–8.38 (dd, J = 1.6 and 2.5 Hz, 1H), 8.21–8.22 (d, J = 2.6 Hz, 1H), 3.18–3.22 (t, 2H), 1.73–1.80 (m, 2H), 1.41–1.50 (m, 2H), 0.92–0.95 (t, 3H). ^{13}C NMR (400 MHz, $CDCl_3$): δ (ppm): 154.2, 146.3, 144.9, 140.2, 32.1, 25.5, 23.0, 13.0. MS (EI, 70 eV) m/z (relative intensity): 218 (5, $[M]^{\cdot+}$, ^{80}Se), 216 (26), 187 (8), 160 (100), 135 (44), 107 (29), 94 (21), 79 (44), 52 (51). *Anal.* Calc. for $C_8H_{12}N_2Se$: C, 44.65, H, 5.62, N, 13.02. Found: C, 44.89, H, 5.79, N, 12.89%.

*2.3.4. 2-(Benzylselenenyl)pyrazine (**7b**)*

(Chloromethyl)benzene (1.74 g, 1.58 mL, 13.75 mmol) was used as the electrophile to obtain **7b** (1.30 g, 44%) as a dark reddish liquid. ^{1}H NMR: (400 MHz, $CDCl_3$): δ (ppm): 8.50–8.51 (d, J = 1.6 Hz, 1H), 8.42–8.43 (dd, J = 1.7 and 2.5 Hz, 1H), 8.24–8.25 (d, J = 2.6 Hz, 1H), 7.34–7.37 (dd, J = 1.5 and 5.1 Hz, 2H), 7.25–7.29 (td, J = 1.5 and 5.1 Hz, 1H), 7.18–7.22 (dd, J = 1.4 and 4.5 Hz, 2H), 4.44 (s, 2H). ^{13}C NMR (400 MHz, $CDCl_3$): δ (ppm): 153.9, 146.2, 144.9, 140.7, 138.3, 129.0, 128.6, 128.5, 128.4, 127.2, 29.1. MS (EI, 70 eV) m/z (relative intensity): 250 (4, $[M]^{\cdot+}$, ^{80}Se), 169 (35), 132 (9), 91 (100), 65 (20), 52 (9). *Anal.* Calc. for $C_{11}H_{10}N_2Se$: C, 52.80, H, 4.00, N, 11.20. Found: C, 52.92, H, 4.06, N, 11.27%.

*2.3.5. Bis(2-pyrazinylselenium)methane (**8b**)*

Diiodomethane (1.80 g, 0.55 mL, 6.87 mmol) was used as the electrophile to generate **8b** (1.13 g, 27%) as a light red solid. M.P. 94–97 °C. ^{1}H NMR: (400 MHz, $CDCl_3$): δ (ppm): 8.66–8.68 (dd, J = 2.5 and 3.8 Hz, 2H), 8.45–8.46 (dd, J = 1.6 and 4.2 Hz, 2H), 8.28–8.30 (dd, J = 2.6 and 5.6 Hz, 2H), 4.85 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 154.1, 146.4, 144.9, 140.2, 14.4. MS (EI, 70 eV) m/z (relative intensity): 332 (2, $[M]^{\cdot+}$, ^{80}Se), 253 (4), 173 (74), 161 (13), 132 (10), 119 (3), 106 (5), 93 (37), 79 (65), 66 (4), 52 (100). *Anal.* Calc. for $C_9H_8N_4Se_2$: C, 32.53, H, 2.40, N, 16.86. Found: C, 32.77, H, 2.51, N, 16.91%.

*2.4. 2,5-Bis(methylselenenyl)pyrazine (**9b**)*

1b (1 g, 12.5 mmol), LDA (27.5 mmol), selenium (2.18 g, 27.5 mmol) and iodomethane (3.90 g, 1.71 mL, 27.5 mmol) were used to obtain **9b** (0.38 g, 12%) as a colorless crystalline solid. M.P. 108–110 °C. ^{1}H NMR: (400 MHz, $CDCl_3$): δ (ppm): 8.40

(s, 2H), 2.45 (s, 6H). ^{13}C NMR (400 MHz, $CDCl_3$): δ (ppm): 148.6, 145.6, 5.5. MS (EI, 70 eV) m/z (relative intensity): 268 (13, $[M]^{\cdot+}$, ^{80}Se), 187 (59), 174 (2), 145 (2), 120 (26), 107 (100), 94 (12), 66 (19), 52 (23). *Anal.* Calc. for $C_6H_8N_2Se_2$: C, 27.08, H, 3.03, N, 10.52. Found: C, 27.19, H, 3.01, N, 10.59%.

2.5. Crystallography

The single crystal X-ray data of compound **9b** was collected on a Bruker SMART Apex II CCD-based diffractometer at 180(2) K using graphite monochromatized Mo Kα radiation (λ = 0.71073 Å). The data reduction was carried out using the SAINT-NT software package from Bruker AXS [27]. The raw intensities were corrected for absorption effects using the multi-scan method with the SADABS [28]. The structure was solved by a combination of direct methods and subsequent difference Fourier syntheses and refined by full matrix least squares on F^2 using the SHELX-2013 suite [29]. The hydrogen atoms were inserted at geometrical positions and refined with isotropic parameters equivalent 1.2 times those of the atom to which they are attached. Anisotropic thermal parameters were used for all non-hydrogen atoms. The ORTEP view was drawn with the OLEX2 [30]. The crystal data and refinement details of **9b** are summarised in Table 1.

Table 1
Crystal data and structure refinement details for **9b**.

Empirical formula	$C_6H_8N_2Se_2$
Formula weight	266.06
Crystal system	triclinic
Space group	$P\bar{1}$
a (Å)	4.09270(10)
b (Å)	5.4402(2)
c (Å)	9.7101(3)
α (°)	84.885(2)
β (°)	83.101(2)
γ (°)	72.689(2)
V (Å^3)	204.583(11)
Z	1
ρ_{calc} (mg/mm^3)	2.160
μ (mm^{-1})	8.961
$F(000)$	126.0
Crystal size (mm^3)	0.32 × 0.26 × 0.1
2θ range for data collection	4.23 to 58.19°
Index ranges	$-5 \leqslant h \leqslant 5$, $-7 \leqslant k \leqslant 7$, $-13 \leqslant l \leqslant 13$
Reflections collected	2390
Independent reflections (R_{int}, R_{sigma})	1090 (0.0169, 0.0214)
Data/restraints/parameters	1090/0/47
Goodness-of-fit (GOF) on F^2	1.139
Final R indexes [$I \geqslant 2\sigma(I)$]	R_1 = 0.0186, wR_2 = 0.0438
Final R indexes (all data)	R_1 = 0.0202, wR_2 = 0.0442
Largest difference in peak/hole (e Å^{-3})	0.47/−0.50

3. Results and discussion

3.1. Synthesis of pyrimidylselenium compounds

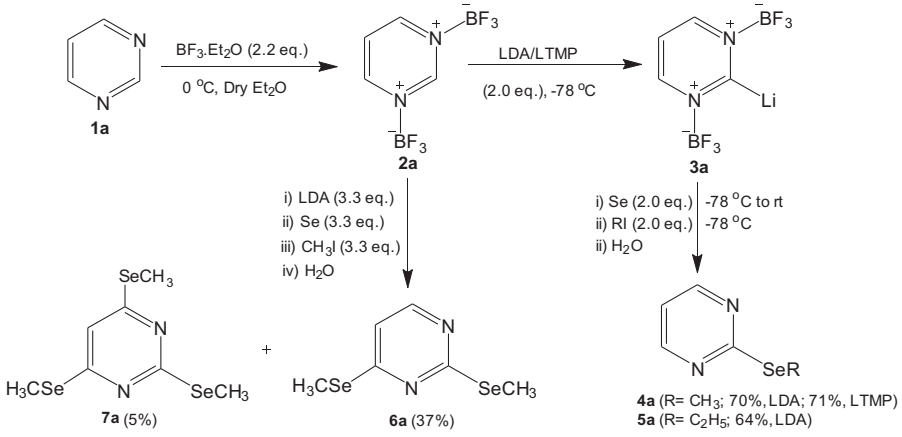
Complexation of **1a** with 1.1 equiv. of $BF_3.Et_2O$ failed to promote the lithiation of **1a** with LDA or LTMP (1.1–2.0 equivs). The use of different solvents (diethyl ether and THF), reaction conditions, and electrophiles (selenium, dimethyl disulfide, benzaldehyde and acetone) did not give the desired products. It appears that the complexation of **1a** with a single BF_3 molecule is not able to generate a stable lithiated species that can participate in the subsequent electrophile quenching reaction.

Next, we investigated the lithiation of **1a** in the presence of 2.2 equiv. of $BF_3{\cdot}Et_2O$. Treatment of **1a** with $BF_3{\cdot}Et_2O$ (2.2 equiv.) and LDA/LTMP (2.0 equiv.) followed by reaction with elemental selenium and iodomethane/iodoethane afforded 2-(methyl/ethylselenenyl)pyrimidine (**4a/5a**) in excellent yields (Scheme 1, Table 2, entries 1–3). The isolation of **4a/5a** establishes the efficient lithiation of **2a** at the C-2 position leading to a stable lithiated species, **3a** (Scheme 1). Based on the inductive and electrostatic effect this position is most likely to get lithiated. We then monitored the effect of the amount of LDA on the lithiation of **2a**. 2,4-Bis (methylselenenyl)pyrimidine (**6a**) and **4a** were obtained when 2.2 equiv. of LDA was used (Table 2, entry 4). The yield of **6a** improved further when we used 3.3 equiv. of LDA (Table 2, entry 5). The later reaction also afforded a triselenated product, **7a**, in a very low yield (Scheme 1). All the synthesized pyrimidylselenium compounds are stable in air and soluble in conventional organic solvents, like THF, diethyl ether, DMF, etc.

3.2. Synthesis of pyrazinylselenium compounds

Contrary to **1a**, BF_3 complexation failed to promote the lithiation of **1b**. Different reaction conditions, like the use of 1.1 or 2.2 equiv. of $BF_3.Et_2O$, LDA or LTMP (1.1/2.2 equiv.) as the lithiating reagents, THF or diethyl ether as the solvents, and different reaction temperatures, had no effect on the outcome of the reaction. A number of electrophiles (selenium, dimethyl disulfide, hexachloroethane, and benzaldehyde) were used but none gave products corresponding to the lithiation of **1b**. It appears that the BF_3 complexation prevents the lithiation of **1b** with LDA or LTMP. As mentioned earlier, the metallation of substituted pyrazinyl derivatives has been achieved through its prior complexation with 1.1 equiv. of $BF_3.Et_2O$ [24]. This indicates that the bimetallic bases and substituents on the pyrazine ring promote the metallation in these moieties.

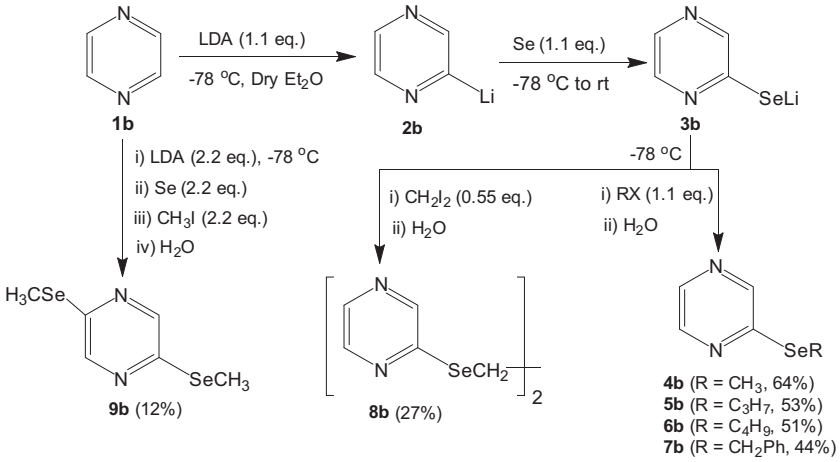
Next, we investigated the direct lithiation of **1b** with LDA as the lithiating reagent. Treatment of **1b** with LDA (1.1 equiv.) at −78 °C



Scheme 1. Synthesis of pyrimidylselenium compounds.

Table 2
Synthesis of selenium derivatives of **1a** and **1b.**

Entry	Substrate	Solvent	$BF_3{\cdot}Et_2O$ (equiv)	Lithiating reagent (equiv)	Electrophile (1.3 equiv)	Product
1.	**1a**	Et_2O	2.2	LDA (2.0)	Se + CH_3I	**4a** (70%)
2.	**1a**	Et_2O	2.2	LTMP (2.0)	Se + CH_3I	**4a** (72%)
3.	**1a**	Et_2O	2.2	LDA (2.0)	Se + C_2H_5I	**5a** (64%)
4.	**1a**	Et_2O	2.2	LDA (2.3)	Se + CH_3I	**4a** (51%), **6a** (21%)
5.	**1a**	Et_2O	2.2	LDA (3.3)	Se + CH_3I	**6a** (37%), **7a** (5%)
6.	**1b**	THF	–	LDA (1.1)	Se + CH_3I	**4b** (64%)
7.	**1b**	THF	–	LDA (1.1)	Se + C_3H_7I	**5b** (53%)
8.	**1b**	THF	–	LDA (1.1)	Se + CH_3I	**6b** (51%)
9.	**1b**	THF	–	LDA (1.1)	Se + C_4H_9I	**7b** (44%)
10.	**1b**	THF	–	LDA (1.1)	Se + CH_2I_2	**8b** (27%)
11.	**1b**	THF	–	LDA (2.2)	Se + CH_3I	**9b** (12%), **4b** (19%)



Scheme 2. Synthesis of pyrazinylselenium compounds.

afforded the carbanion **2b** (Scheme 2). The reaction of **2b** with selenium gave the selenolate anion, **3b**, which on quenching with iodomethane (1.1 equiv.) afforded 2-(methylselenenyl)pyrazine (**4b)** in a 64% yield. Similarly, a variety of 2-pyrazinylselenium compounds were synthesized by reacting **3b** with different electrophiles (Table 2, entries 6–10). The dilithiation of **1b** was attempted with 2.2 equiv. of LDA at −78 °C. Subsequent reaction with elemental selenium and iodomethane (2.2 equiv.) afforded 2,5-bis(methylselenenyl)pyrazine (**9b**) and **4b** in 12% and 19% yields, respectively (Scheme 2). All the synthesized pyrazinylselenium compounds are stable under normal environmental conditions and do not require special handling procedures.

3.3. Spectroscopic studies

The ^{1}H NMR spectrum of **4a** contains a doublet at δ 8.61–8.60 (J = 4.8 Hz) ppm due to H-6 and H-4 ring protons. The H-5 signal appears as a triplet at δ 7.23–7.25 (J = 4.8 Hz) ppm. The spectrum of **6a** contains two doublets in the range δ 7.94–7.96 (J = 5.2 Hz) and 6.91–6.92 (J = 5.4 Hz) ppm that suggests the dilithiation of **1a** at the C-2 and C-4 position. The spectra of the pyrazinylseleniums (**4b-8b**) have lower coupling constant values than the pyrimidyl derivatives. The H-5 signals in these compounds appear downfield ($\sim\delta$ 8.40 ppm) due to its proximity to the nitrogen atom. The signal corresponding to the –SeCH_3 protons in the pyrimidyl (**4a** and **6a**) and pyrazinyl (**4b** and **9b**) derivatives appears as singlet in the δ 2.39–2.47 ppm range. In the ^{13}C NMR spectra of the pyrimidylseleniums, the C-2 signal appears downfield than the corresponding pyrazinyl derivatives. For example, in **4a** the C-2 signal is observed at δ 169.0 ppm, whereas it appears at δ 154.1 ppm in **4b**. The –SeCH_3 signals in **4a** and **4b** appear at δ 6.4 and 5.3 ppm, respectively. The compound **6a** has two non-equivalent –SeCH_3 units, which is evident from the signals at δ 6.7 (–SeCH_3 at C-2) and δ 5.2 (–SeCH_3 at C-4) ppm. Conversely, the compound **9b** has two equivalent –SeCH_3 carbons that resonate at δ 5.5 ppm The mass spectrum of **4a** shows the molecular ion $[C_5H_6N_2\ ^{80}Se]^{+\cdot}$ peak at m/z 174 due to the loss of an electron from the molecule that contains the most abundant ^{80}Se isotope. The base ion peak is observed at m/z 94 due to the fragment $[C_5H_6N_2]^+$ formed by the loss of ^{80}Se radical from the molecular ion. Similar to **4a**, the mass spectrum of **4b** displays the base ion peak at m/z 94. The mass spectrum of **6a** shows the molecular ion peak at m/z 268. The loss of Se and $[SeCH_3]^+$ fragments from the molecular ion gives the base ion peak at m/z 93.

3.4. Solid state structural features of *9b*

The position of the second –SeCH_3 unit in **9b** was determined by single crystal X-ray crystallography as the NMR spectral data was inconclusive. The crystals of **9b** were grown in a solution of hexane and ethyl acetate. In the solid state, the individual molecules of **9b** display a centrosymmetric structure with the inversion center located in the middle of the aromatic ring leading to two independent C–N and Se–C distances and one single C–C distance. Their lengths are given in Table 3 together with selected angles involving the selenium center. An ORTEP view of **9b** with the crystallo-

Table 3
Selected bond distances (Å) and angles (°) for compound **9b**.

Se(21)–C(2)	1.907(2)	Se(21)–C(22)	1.935(2)
N(1)–C(2)	1.332(2)	N(1)–C(2)	1.338(2)
C(2)–C(3a)	1.388(3)		
C(2)–Se(21)–C(22)	98.08(8)	N(1)–C(2)–Se(21)	119.14(13)
C(2)–Se(21)–C(22)	119.08(14)		

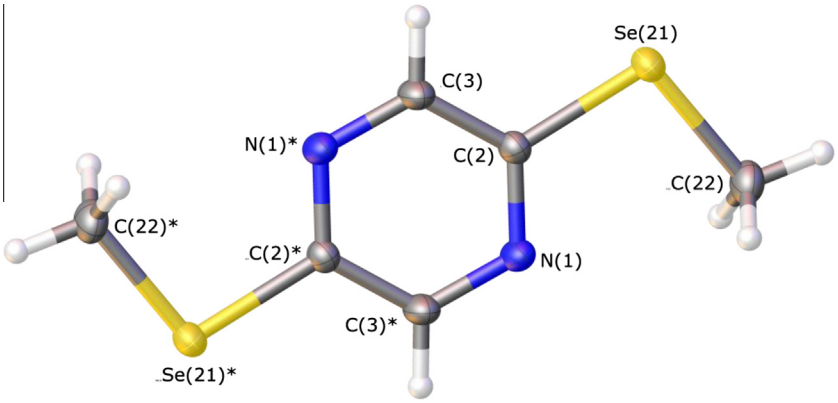


Fig. 1. ORTEP view of **9b** with thermal ellipsoids drawn at the 50% probability level and showing the atom numbering scheme adopted, in which * denotes the symmetry operator $1 - x, -y, -z$.

graphic notation scheme used is shown in Fig. 1. The compound **9b** has the shortest Se–C(sp^2) bond lengths (1.907(2) Å) among all the reported bis(methylselenenyl) derivatives [26,31,32]. However, the two Se–C(sp^3) bond lengths are similar to that of bis(methylselenenyl) derivatives [26,31,32]. In the crystal structure each nitrogen atom of the pyrazine ring is involved in C–H···N hydrogen bonds with C···N distances of 3.392 Å and C–H···N angles of 142°. No significant intermolecular Se···Se secondary interactions were observed in the crystal structure.

4. Conclusion

In conclusion, we have reported an effective lithiation of the pyrimidine ring through its complexation with 2.2 equiv. of BF_3·Et_2O. The developed methodology provides a convenient pathway to synthesize a variety of pyrimidylselenium compounds. The synthesis of pyrazinylselenium compounds was achieved by the direct lithiation route as the BF_3-complexation could not facilitate the lithiation of the pyrazine ring.

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Appendix A. Supplementary material

CCDC 1001267 contains the supplementary crystallographic data for **9b**. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif. Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.ica.2014.06.025.

References

[1] C.A. Collins, F.H. Fry, A.L. Holme, A. Yiakouvaki, A. Al-Qenaei, C. Pourzand, C. Jacob, Org. Biomol. Chem. 3 (2005) 1541.
[2] K. Kloc, I. Maliszewska, J. Młochowski, Synth. Commun. 33 (2003) 3805.
[3] A. Molter, G.N. KaluCerović, H. Kommera, R. Paschke, T. Langer, R. Pöttgen, F. Mohr, J. Organomet. Chem. 701 (2012) 80.
[4] R.F. Schinazi, J. Arbiser, J.J.S. Lee, T.I. Kalman, W.H. Prusoffi, J. Med. Chem. 29 (1986) 1293.
[5] G. Zhao, H. Lin, S. Zhu, H. Sun, Y. Chen, Anticancer Drug Des. 13 (1998) 769.
[6] R.K. Sharma, G. Kedarnath, V.K. Jain, A. Wadawale, C.G.S. Pillai, M. Nalliath, B. Vishwanadh, Dalton Trans. 40 (2011) 9194.
[7] Y. Cheng, T.J. Emge, J.G. Brennan, Inorg. Chem. 35 (1996) 7339.
[8] S. Dey, V.K. Jain, J. Singh, V. Trehan, K.K. Bhasin, B. Varghese, Eur. J. Inorg. Chem. (2003) 744.
[9] D.M. Browne, O. Niyomura, T. Wirth, Org. Lett. 9 (2007) 3169.
[10] J. Burés, M. Martín, F. Urpí, J. Vilarrasa, J. Org. Chem. 74 (2009) 2203.
[11] G. Kedarnath, V.K. Jain, Coord. Chem. Rev. 257 (2013) 1409.
[12] J.S. Dhau, A. Singh, A. Singh, B.S. Sooch, Phosporus Sulfur Relat. Elem. 189 (2014) 687.
[13] C.P. Prabhu, P.P. Prasad, A.P. Wadawale, K.I. Priyadarsini, V.K. Jain, J. Organomet. Chem. 713 (2012) 42.
[14] J.S. Dhau, R. Dhir, A. Singh, J. Organomet. Chem. 696 (2011) 2406.
[15] K.K. Bhasin, V. Arora, Appl. Organomet. Chem. 18 (2004) 359.
[16] K.K. Bhasin, E. Arora, K. Kaur, S.K. Kang, M. Gobel, T.M. Klapoetke, S.K. Mehta, Tetrahedron 65 (2009) 247.
[17] K.K. Bhasin, E. Arora, S.K. Mehta, T.M. Klapoetk, J. Organomet. Chem. 696 (2011) 835.
[18] A.S. Hodage, P.C. Parashiva, Prasad.P. Phadnis, A. Wadawale, K.I. Priyadarsini, V.K. Jain, J. Organomet. Chem. 720 (2012) 19.
[19] R.K. Sharma, A. Wadawale, G. Kedarnath, B. Vishwanath, V.K. Jain, Inorg. Chim. Acta 411 (2014) 90.
[20] R.S. Chauhan, R.K. Sharma, G. Kedarnath, D.B. Cordes, A.M.Z. Slawin, V.K. Jain, J. Organomet. Chem. 717 (2012) 180.
[21] R.K. Sharma, A. Wadawale, G. Kedarnath, D. Manna, T.K. Ghanty, B. Vishwanadh, V.K. Jain, Dalton Trans. 43 (2014) 6525.
[22] N. Plé, A. Turck, K. Couture, G. Quéguiner, J. Org. Chem. 60 (1995) 3781.
[23] A. Turck, N. Plé, F. Mongin, G. Quéguiner, Tetrahedron 57 (2001) 4489.
[24] K. Groll, S.M. Manolikakes, X.M. Jourdin, M. Jaric, A. Bredihhin, K. Karaghiosoff, T. Carell, P. Knochel, Angew. Chem., Int. Ed. 52 (2013) 6776.
[25] D.D. Perrin, W.L.F. Armarego, Purification of Laboratory Chemicals, third ed., Pergamon Press, Oxford, 1988.
[26] J.S. Dhau, A. Singh, R. Dhir, J. Organomet. Chem. 696 (2011) 2008.
[27] Bruker SAINT-plus Bruker AXS Inc., Madison, Wisconsin, USA. 2007.
[28] G.M. Sheldrick, SADABS, University of Göttingen, Germany, 1996.
[29] G.M. Sheldrick, Acta Crystallogr., Sect. A 64 (2008) 112.
[30] O.V. Dolomanov, L.J. Bourhis, R.J. Gildea, J.A.K. Howard, H. Puschmann, J. Appl. Crystallogr. 42 (2009) 339.
[31] J.S. Dhau, A. Singh, A. Singh, B.S. Sooch, P. Brandão, V. Félix, Inorg. Chim. Acta 392 (2012) 335.
[32] J.S. Dhau, R. Dhir, A. Singh, P. Brandão, V. Félix, Inorg. Chim. Acta 404 (2013) 108.