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SELENIUM HETEROCYCLES XXXX [1]. SYNTHESES OF 4- (2-*PYRAZINYL*) - *1, 2, 3*- SELENADIAZOLE AND 4- (2-PYRAZILYL) - 1, 2, 3- THIADIAZOLE

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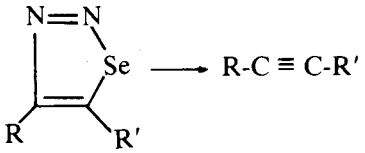
Abstract

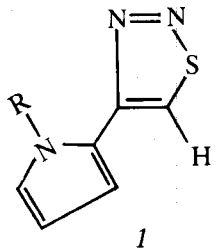
Reaction of thionyl chloride with 2-acetyl-1- benzenesulfonylpyrrole semicarbazone (**6 c**) gave 4 - (1- benzenesulfonyl -2 - pyrrolyl) - 1, 2, 3 -thiadiazole (**1c**). Selenium dioxide oxidation of 2-acetylpyrazine semicarbazone (**10**) in acetic acid afforded 4- (2-pyrazinyl) - 1, 2, 3- selenadiazole (**4**). Reaction of thionyl chloride with compound **10** gave 4- (2-pyrazinyl) - 1, 2, 3- thiadiazole (**3**). Base catalized decomposition of **4** afforded the *cis*-fulvene **13**. Similarly, reaction of **3** with a base gave the corresponding *cis*-fulvene **11**. Heating compounds **11** or **13** gave respectively the corresponding *trans* isomers **12** or **14**.

Introduction

In previous papers [2-5] the synthesis of 1, 2, 3- selenadiazoles and the utility of this heterocyclic ring system for the preparation of alkynes was reported.



The utility of this reaction was demonstrated by the synthesis of different type of 4 - aryl - 1, 2, 3 - selenadiazoles [6]. In continuation of our study on the chemistry of sulfur and selenium heterocyclic compounds [7-9] the syntheses of 4- (2-pyrrolyl) 1, 2, 3- thiadiazole (**1**), 4- (2-pyrrolyl) 1, 2, 3- selenadiazole (**2**), 4- (2-pyrazinyl) 1, 2, 3- thiadiazole (**3**), and 4- (2-pyrazinyl) 1, 2, 3- selenadiazole (**4**) were attempted.



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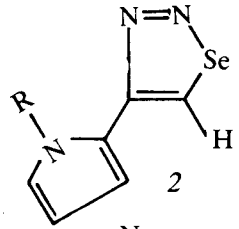

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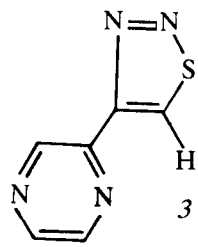

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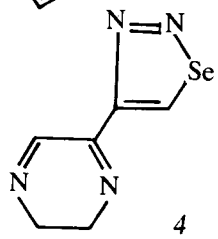


4

a = R =H
b = R =CH_3
c = R = SO_2Ph

Key words: Selenium Heterocycles, Pyrazinyl 1, 2,3- Selenadiazole, Pyrazilyl 1, 2, 3- Thiadiazole

Results and Discussion

The syntheses of compounds **1** and **2** were attempted according to the Scheme 1.

Reaction of 2-acetylpyrrole (**5a**) [10] with semicarbazide afforded 2-acetylpyrrole semicarbazone (**6a**). However the reaction of compound **6a** with either thionyl chloride of selenium dioxide, according to our procedures reported previously [2,8], did not afford the corresponding 1, 2, 3 - thiadiazole (**1a**) or 1, 2, 3 — selenadiazole (**2 a**). We thought that the N-H of pyrrole prevented the success of the reaction. Therefore, we started the same sequence from 2-acetyl-1- methylpyrrole [**5b**] [11]. Reaction of compound **5b** with semicarbazide gave the corresponding semicarbazone (**6b**). Oxidation of the latter with selenium dioxide did not give compound **2b**. NMR of the mixture showed that there was no N-CH_3 in the product. Therefore, it seemed to us that selenium dioxide at first oxidized N-CH_3 group to N-H and then the compound was further decomposed by selenium dioxide. The reaction of compound **6b** with thionyl chloride did not give compound **1b**.

Finally we started from a better protection group namely, 2- acetyl-1- benzenesul fonylpyrrole [**5c**] [12]. Reaction of thionyl chloride with the semicarbazone **6c** gave 4- (1- benzenesulfonyl – 2– pyrrolyl) 1, 2, 3 - thiadiazole (**1c**). However the reaction of selenium dioxide with **6c** did not afford the corresponding selenadiazole **2c**.

The syntheses of 4- (2-pyrazinyl) 1, 2, 3- thiadiazole (**3**) and 4- (2-pyrazinyl) 1, 2, 3- selenadiazole (**4**) were accomplished according to Scheme 2.

Reaction of diazomethane with 2 - formylpyrazine (**7**) [13] gave 2 - acetylpyrazine. However, the yield was low and unsatisfactory. Therefore, we prepared compound **9** through the reaction of methylmagnesium iodide with 2- cyanopyrazine (**8**) [14] in good yield.

Reaction of compound **9** with semicarbazide gave 2-acetylpyrazine semicarbazone (**10**). Reaction of thionyl chloride with compound **10** yielded compound **3**. Selenium dioxide oxidation of compound **10** in acetic acid afforded the desired compound **4**.

Since molecular charge-transfer complexes of tetrathiafulvalene or its selenium analog, tetraselensfulvalene with tetracycnoquinodimethane behave electrically and optically like one - dimensional metals [15, 16] we became interested in the syntheses of di - (2-pyrazinyl) - 1, 4- dithiafulvene and its corresponding selenium analog as a possible donor in the above complex.

Addition of potassium hydroxide pellets to the alcoholic solution of compound **3** gave *cis*-2, W-di - (2 - pyrazinyl) - 1, 4- dithiafulvene (**11**) which was isomerized to the corresponding *trans* isomer (**12**) through heating [17]. Similarly, reaction of a base with compound **4** afforded *cis*-2, w-di - (2-pyrazinyl) 1, 4-diselenafulvene (**13**). The latter could be isomerized to the *trans* isomer (**14**) through heating. The study of the possible complex formation of compounds **11, 12, 13** and **14** with tetracyanoquinodimethane is under investigation. The structure of all compounds prepared was confirmed by analytical and spectroscopic methods.

Experimental Section

Melting points were determined on a Kofler hot stage apparatus and are uncorrected. The IR spectra were obtained using a Perkin - Elmer Model 267 spectrograph (potassium bromide disks). The nmr spectra were recorded on a Varian T-60A spectrometer and chemical shifts (δ) are in ppm relative to internal tetramethylsilane. Mass spectra were run on a Varian Model MAT MS- 311 spectrometer at 70 ev.

2- Acetylpyrrole Semicarbazone (**6a**).

To a solution of 2- acetylpyrrole (**5a**, 1.09g, 0.01 mol) in ethanol (15ml) a solution of semicarbazide hydrochloride (1.13g) and sodium acetate (1.23g) in water (5 ml) was added. The mixture was heated on a water bath until the precipitate was complete (15 minutes). The precipitate was filtered to give 1.0g (60 %) of **6a**; m.p. 188-190°C.

Anal. Calcd. for $C_7H_{10}N_4O$: C, 50.60; H, 6.02; N, 33.73. Found: C, 50.79; H, 6.18; N, 33.62.

2- Acetyl -1- methylpyrrole Semicarbazone (**6b**).

This compound was prepared similar to **6a** in 65% yield; m.p. 214- 216°C.

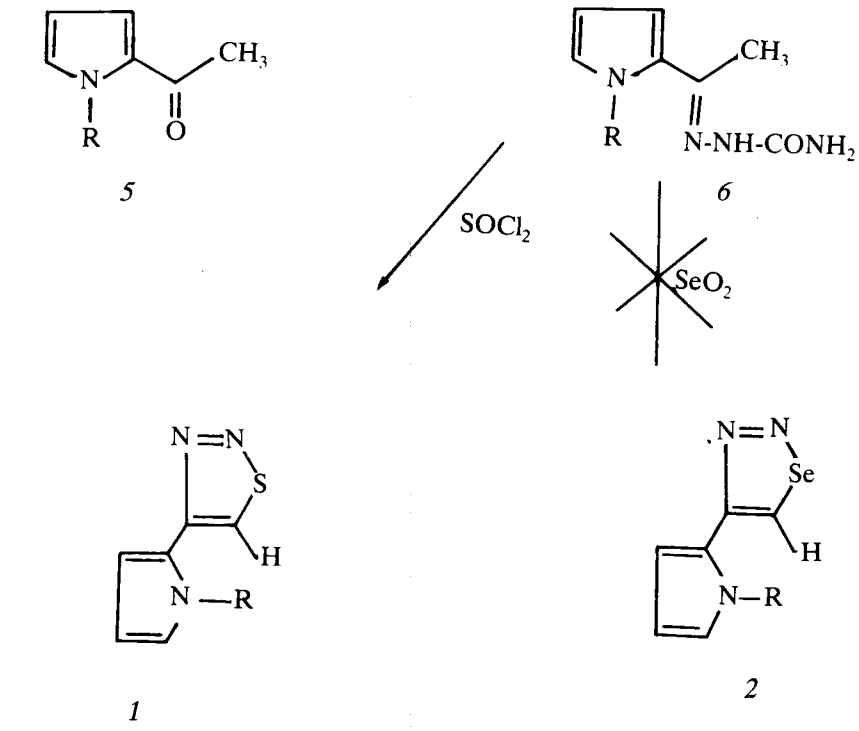
Anal. Calcd. for $C_8H_{12}N_4O$: C, 53.33; H, 6.66; N, 31.11. Found: C, 53.17; H, 6.48; N, 31.03.

2- Acetyl -1- benzenesulfonylpyrrole Semicarbazone (**6c**).

This compound was prepared similar to **6a** in 70% yield; m.p. 203- 205°C.

Anal. Calcd. for $C_{13}H_{14}N_4O_3S$: C, 50.98; H, 4.58; N, 18.30. Found: C, 51.03; H, 4.39; N, 18.23.

4- (1- Benzensulfonyl- 2- pyrrolyl) - 1, 2, 3- thiadiazole (**1c**).



5 *6* *1* *2*

a = R = H
b = R = CH_3
c = R = $C_6H_5SO_2$

Scheme 1

To compound **6c** (3.06g, 0.01 mol) was added thionyl chloride (15 ml). The mixture was heated on a water bath at 60°C. After gas evolution ceased, the mixture was cold. Chlorofrom was added (50 ml) and the mixture was decomposed with ice - cold concentrated sodium carbonate solution. The organic layer was washed with water and dried with anhydrous sodium sulfate. After evaporation of the solvent the residue was crystallized from ether to give 1.33g (45%) of **1c**; m.p. 129- 130°C; IR: 3080, 1500, 1470 (aromatic), 1370 and 1150 (SO_2); NMR ($CDCl_3$): 7.86 (s, 1H, H_5); 7.56 (m, 5H, C_6H_5), 6.50 (m, 3H, aromatic); MS: m/e (%): 291 (M^+, 67), 263 (10), 214 (44), 122 (100) and 110 (90).

2- Acetylpyrazine (**9**).

Method A:

To a stirred solution of 2 - formylpyrazine (**7**, 1.08g. 0.01 mol) [15] in ether (10 ml) a solution of diazomethane (0.42g, 0.01 mol) in ether (30 ml) at r.t. was added. The progress of the reaction was followed by TLC. When the reaction was complete, the ether was evaporated. The residue was purified by preparative TLC on silica gel using chloroform - methanol (95:1) as eluent. The fast moving fraction was crystallized from ether to give 0.12g (10%) of **9**; m.p. 74- 75°C.

Anal. Calcd. for $C_6H_6N_2O$: C, 59.02; H, 4.92; N, 22.95. Found: C, 59.15; H, 5.04; N, 22.81.

Method B:

Compound **9** was prepared according to reference [14] in 65% yield;

2- Acetylpyrazine Semicarbazone (**10**).

This compound was prepared silmilar to **6a** in 90% yield; m.p. 218- 220°C.

Anal. Calcd. for $C_7H_9N_5O$: C, 46.93; H, 5.02; N, 39.11. Found: C, 46.81; H, 5.19; N, 39.02.

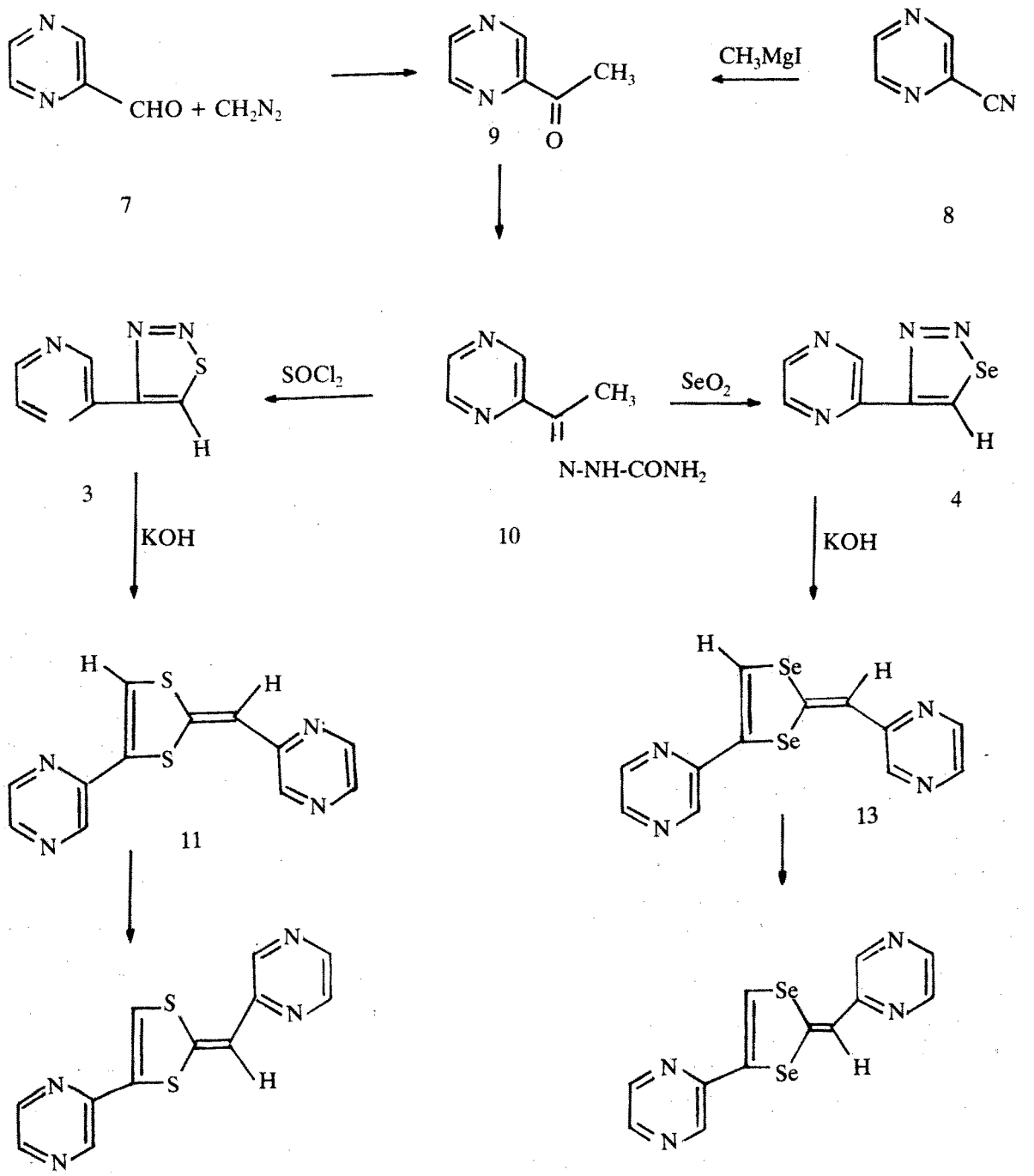
4- (2- pyrazinyl) - 1, 2, 3- thiadiazole (**3**)

This compound was prepared similar to **1c** in 70% yield; m.p. 162- 163°C (ether); NMR ($CDCl_3$): 9.75 (s, 1H, H_5 of thiadiazole), 9.29 (s, 1H, H_3 of pyrazine) and 8.68 (s, 2H, $H_{5,6}$ of pyrazine); MS: m/e (%) 164 (M^+, 10), 136 (100), 109 (30), 83 (78) and 32 (17).

Anal. Calcd. for $C_6H_4N_4S$: C, 43.90; H, 2.44; N, 34.15. Found: C, 43.76; H, 2.31; N, 34.01

4- (2- Pyrazinyl) - 1, 2, 3- selenadiazole (4).

2- Acetylpyrazine semicarbazone (1.79g, 0.01 mol)



7 9 8 3 10 4 11 13 12 14

Scheme 2

was dissolved in 25 ml of acetic acid. To the hot solution, selenium dioxide powder (1.1g, 0.01 mol) was added and the reaction mixture was stirred until the vigorous reaction ceased. The solvent was evaporated. The chromatography of the residue on small silica gel column using chloroform as eluent to give 1.27g (60%) of 4 m.p. 158- 159°C (ether); NMR ($CDCl_3$): 10.12 (s, 1H, H_5 of selenadiazole), 9.68 (s, 1H, H_3 of pyrazine) and 8.60 (s, 2H, $H_{5,6}$ of pyrazine); MS: m/e (%) 211 (M^+, 9), 184 (90), 167 (21), 157 (25), 149 (32), 131 (43), 104 (33), 92 (40), 79 (61), 52 (100), 50 (63) and 37 (21)

Anal. Calcd. for $C_6H_4N_4Se$: C, 34.12; H, 1.90; N, 26.54, Found: C, 34.01; H, 2.02; N, 26.38.

cis-2, w-Di (2- Pyrazinyl) - 1, 4- dithiafulvene (**11**)

Compound 3 (0.82g, 5 mmol) was dissolved in 20 ml of 95% of ethanol and a few pellets of potassium hydroxide was added. After gas evolution ceased, potassium hydroxide pellets were removed, crystals were filtered, and recrystallized from ethanol to give 0.4 g (60%) of **11**; m.p. 224- 226°C; MS: m/e (%) 272 (M^+, 45), 222 (25), 168 (15), 136 (15) and 72 (100).

Anal. Calcd for $C_{12}H_8N_4S_2$: C, 52.94; H, 2.94; N, 20.59. Found: C, 52.79; H, 2.81; N, 20.71

cis-2, w-Di - (2- pyrazinyl) - 1, 4- diselenafulvene (**13**).

This compound was prepared similar to **11** in 70% yield; m.p. 134- 136°C (ethanol); MS: m/e (%) 366 (M^+, 100), 263 (73), 183 (24), 160 (15) and 104 (10).

Anal. Calcd. for $C_{12}H_8N_4Se_2$: C, 39.34; H, 2.19; N, 15.30. Found: C, 39.46; H, 2.04; N, 15.16.

trans-2, w-Di - (2- pyrazinyl) - 1, 4- dithiafulvene (**12**).

Compound **11** (272 mg, 1 mmol) was heated at 230°C for 5 minutes. After cooling the mass was crystallized from ethanol to give 245 mg (90%) of **12**; m.p. 288- 290°C.

Anal. Calcd. for $C_{12}H_3N_4S_2$: C, 52. 94; H, 2.94; N, 20.59. Found: C, 52.85; H, 2.81; N, 20.46.

trans-2, w- Di - (2- pyrazinyl)- 1, 4- diselenafulvene (**14**).

This compound was prepared similar to **12** in 90% yield; m.p. 210- 212°C (ethanol).

Anal Calcd for $C_{12}H_8N_4Se_2$: C, 39.34; H, 2.19; N, 15.30. Found: C, 39.45; H, 2.23; N, 15.43.

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