Selenium Heterocycles. XXXVII [1]. Synthesis of 4-(Thiazol-4-yl)-1,2,3-selenadiazoles and 4-(Selenazol-4-yl)-1,2,3-selenadiazoles

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Starting from readily available 2-substituted-4-formylthiazoles and selenazoles, a series of 4-(2-aryl-4-selenazolyl)-1,2,3-selenadiazoles I and 4-(2-substituted-4-thiazolyl)-1,2,3-selenadiazoles II were prepared. Pyrolysis of compound II afforded (2-substituted-4-thiazolyl) acetylenes VII. Addition of potassium hydroxide pellets to an alcoholic solution of II gave 2-substituted-1,4-diselenafulvenes VIII. Decomposition of compound II with base followed by the addition of carbon disulfide gave 5-substituted 2-thioxo-1,3-thiaselenoles XI.

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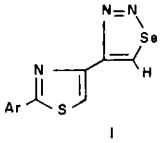
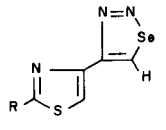
In continuation of the study on the chemistry of selenium heterocyclic compounds [2-8] and as a part of a program designed to expand the chemistry of 1,2,3-selenadiazole to 4-heteroaryl-1,2,3-selenadiazole, it became necessary to prepare 4-(2-aryl-4-selenazolyl)1,2,3-selenadiazoles I and 4-(2-substituted-4-thiazolyl)1,2,3-selenadiazoles II.



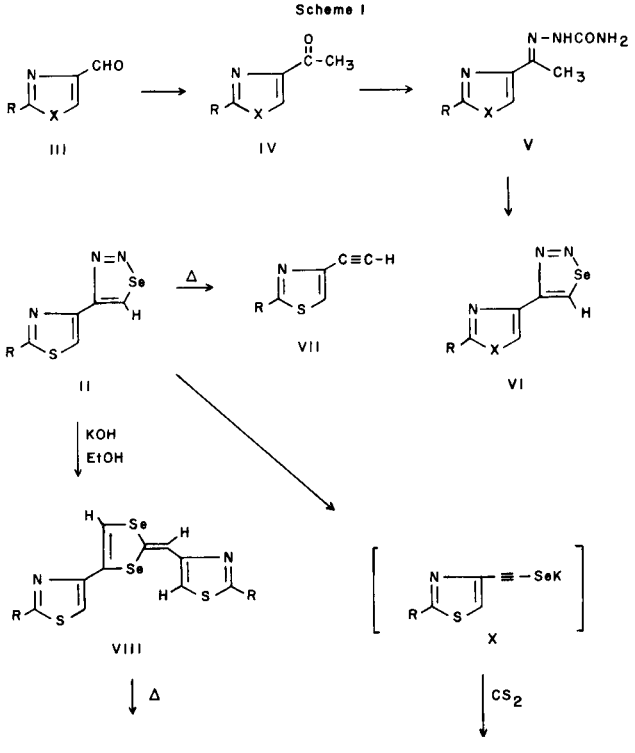
I



II

Compounds I and II could be prepared according to Scheme I.

Scheme I



For the preparation of 2-aryl-4-acetylselenazoles IV (R = aryl, X = Se) the reaction of diazomethane with the aldehyde III (R = aryl, X = Se) [9] was studied.

It has been reported that in substituted benzaldehyde the speed of the reaction of diazomethane with aldehyde depends on the nature of the substituents [10-11].

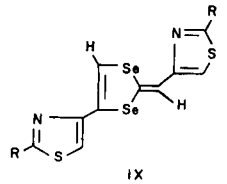
We have also observed that the duration of the reaction of the aldehyde III with diazomethane depends on the nature of the substituents. Indeed, the reaction of *p*-chloro- and *p*-bromophenyl derivatives were longer than other compounds.

Selenium dioxide oxidation of the semicarbazones V [2] in acetic acid gave the desired compound V in high yield.

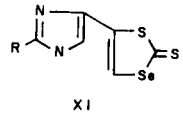
Pyrolysis of compounds II afforded acetylenes VII in good yield.

Addition of potassium hydroxide pellets to the alcoholic solution of II gave *cis*-1,4-diselenafulvene (VIII). This observation was similar to the one reported previously [3]. The nmr spectrum of VIIIa (R = CH_3) was in accordance with the suggested structure. In the low field part of the spectrum H3 and Hω appeared as singlets at 7.70 and 6.80 ppm respectively. Heating the *cis* isomer to 200° for 15 minutes converted the *cis*-isomer to *trans*-1,4-diselenafulvene (IX).

Decomposition of compound II with ethanolic potassium hydroxide and subsequent addition of carbon disulfide in tetrahydrofurane afforded 5-substituted 2-thioxo-1,3-thiaselenoles XI.

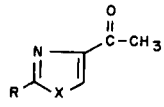


IX



XI

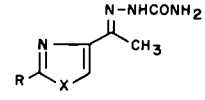
Table I



Compound No.	R	X	Mp °C [a]	Yield	Formula	C % Calcd.	C % Found	H % Calcd.	H % Found	N % Calcd.	N % Found
IVa	C_6H_5	Se	60-61	70	$C_{11}H_9NOSe$	52.80	52.69	3.60	3.75	5.60	5.47
IVb	p-$CH_3C_6H_4$-	Se	36-37	72	$C_{12}H_{11}NOSe$	54.55	54.39	4.17	4.05	5.30	5.45
IVc	p-$CH_3OC_6H_4$	Se	74-76	65	$C_{12}H_{11}NO_2Se$	51.43	51.30	3.93	3.82	5.00	5.16
IVd	p-ClC_6H_4-	Se	68-70	60	$C_{11}H_8ClNOSe$	46.40	46.55	2.82	2.95	4.92	4.99
IVe	p-BrC_6H_4	Se	83-85	60	$C_{11}H_8BrNOSe$	40.12	40.01	2.43	2.56	4.26	4.09
IVf	C_6H_5	S	87-89 [b]	50	$C_{11}H_9NOS$	65.02	65.18	4.43	4.56	6.90	7.08
IVg	CH_3	S	55-57	40	C_6H_7NOS	51.06	51.18	4.96	4.83	9.93	9.78

[a] All compounds were crystallized from ether. [b] Reference [12] mp 90-91°.

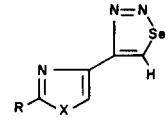
Table II



Compound No.	R	X	Mp °C [a]	Yield	Formula	C % Calcd.	C % Found	H % Calcd.	H % Found	N % Calcd.	N % Found
Va	C_6H_5-	Se	197-199	90	$C_{12}H_{12}N_4OSe$	46.91	46.80	3.91	3.87	18.24	18.07
Vb	p-$CH_3C_6H_4$-	Se	208-210	95	$C_{13}H_{14}N_4OSe$	48.60	48.74	4.36	4.44	17.45	17.34
Vc	p-$CH_3OC_6H_4$-	Se	194-196	85	$C_{13}H_{14}N_4O_2Se$	46.29	46.43	4.15	4.22	16.62	16.74
Vd	p-ClC_6H_4-	Se	198-200	90	$C_{12}H_{11}ClN_4OSe$	42.17	42.02	3.22	3.36	16.40	16.51
Ve	p-BrC_6H_4-	Se	209-211	90	$C_{12}H_{11}BrN_4OSe$	37.31	37.31	2.85	2.71	14.51	14.59
Vf	C_6H_5-	S	208-210	95	$C_{12}H_{12}N_4OS$	55.38	55.19	4.62	4.51	21.54	21.38
Vg	CH_3-	S	184-186	90	$C_7H_{10}N_4OS$	42.42	42.35	5.05	5.16	28.28	28.09

[a] All compounds were crystallized from ethanol.

Table III



Compound No.	R	X	Mp °C [a]	Yield	Formula	C % Calcd.	C % Found	H % Calcd.	H % Found	N % Calcd.	N % Found
VIa	C_6H_5	Se	93-94	80	$C_{11}H_7N_3Se_2$	38.94	39.01	2.06	2.19	12.39	12.43
VIb	p-$CH_3C_6H_4$-	Se	108-110	80	$C_{12}H_9N_3Se_2$	40.79	40.93	2.55	2.64	11.90	12.04
VIc	p-$CH_3OC_6H_4$-	Se	143-144	85	$C_{12}H_9N_3OSe_2$	39.02	39.16	2.44	2.37	11.38	11.26
VId	p-ClC_6H_4-	Se	165-167	87	$C_{11}H_6ClN_3Se_2$	35.34	35.42	1.61	1.69	11.24	11.09
VIe	p-BrC_6H_4-	Se	155-157	88	$C_{11}H_7BrN_3Se_2$	31.58	31.73	1.44	1.36	10.05	10.13
VIf	C_6H_5	S	122-124	70	$C_{11}H_7N_3SSe$	45.21	45.09	2.40	2.28	14.39	14.46
VIg	CH_3	S	119-121	50	$C_6H_5N_3SSe$	31.30	31.21	2.17	2.04	18.26	18.38

[a] All compounds were crystallized from ether.

EXPERIMENTAL

Melting points were determined on Kofler hot stage apparatus and are uncorrected. The ir spectra were obtained using a Perkin-Elmer Model 267 spectrograph (potassium bromide discs). The nmr spectra were recorded on a Varian T-60 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.

4-Acetyl-2-methylthiazole (IVg).

To a stirred solution of 4-formyl-2-methylthiazole [9] (IIIg, 1.27 g, 0.01 mole) in chloroform (10 ml), at ambient temperature, a solution of diazomethane (0.42 g, 0.01 mole) in ether was added. The stirring was continued and the progress of the reaction monitored by tlc. After the completion of the reaction, the solvent was distilled off and the residue was purified by tlc on silica gel using chloroform-ethylacetate (90:10) as eluent. The desired compound was crystallized from ether to give 0.56 g (40%) of IVg, mp 55-57°; ir: 1680 cm^{-1} (CO); nmr (deuteriochloroform): 8.0 (s, 1H, H5), 2.77 (s, 3H, CH_3) and 2.64 ppm (s, 3H, CH_3CO); ms: m/e (%) 141 (M^+, 71), 126 [M-(CH_3CN), 12], 99 [M-(CH_3CO), 19], 98 [M-(CH_2CO), 16], 85 [M-(CH_3CN and CH_3), 11], 52 (32), 57 (36) 45 (21), 43 (57) and 32 (28).

Anal. Calcd. for C_6H_7NOS: C, 51.06; H, 4.96; N, 9.93. Found: C, 51.18; H, 4.83; N, 9.78.

Other 2-substituted-4-acetylthiazoles and selenazoles IVa-IVf were prepared similarly (see Table I).

4-Acetyl-2-methylthiazole Semicarbazone (Vg).

To a solution of IVg (1.41 g, 0.01 mole) in ethanol (20 ml) a solution of semicarbazide hydrochloride (1.11 g, 0.01 mole) and sodium acetate (1.5 g) in water (4 ml) was added. The mixture was let to stand at ambient temperature overnight and the precipitate was filtered to give 1.78 g (90%) of Vg, mp 184-186°; ir: 3340 (NH_2), 3180 (NH) and 1690 cm^{-1} (CO).

Anal. Calcd. for $C_7H_{10}N_4OS$: C, 42.42; H, 5.05; N, 28.28. Found: C, 42.35; H, 5.16; N, 28.09.

Other 2-substituted-4-acetylthiazoles and selenazoles semicarbazones Va-Vf were prepared similarly.

4-(2-Methyl-4-thiazolyl)1,2,3-selenadiazoles (VIg).

To a solution of compound Vg (1.98 g, 0.01 mole) in glacial acetic acid (50 ml) selenium dioxide powder (1.11 g, 0.01 mole) was added. The mixture was warmed gently on a water bath to start the reaction (gas evolution). Stirring was continued until the gas evolution ceased (*ca.* 15 minutes). The reaction mixture was filtered and the solvent evaporated under the reduced pressure. The residual product purified by tlc on silica gel using chloroform as eluent to give 1.15 g (50%) of VIg; nmr (deuteriochloroform): 9.70 (s, 1H, H_5), 8.0 (s, 1H, aromatic) and 2.80 ppm (s, 3H, CH_3); ms: m/e (%) 231 (M^+, 37), 229 (19), 203 (98), 201 (44), 162 (78), 160 (37), 123 (13), 118 (59), 110 (30), 82 (100), 69 (30), 45 (33) and 38 (30).

Anal. Calcd. for $C_6H_5N_3SSe$: C, 31.30; H, 2.17; N, 18.26. Found: C, 31.21; H, 2.04; N, 18.38.

Other 4-(2-substituted-4-thiazolyl)-1,2,3-selenadiazoles and 4-(2-substituted-4-selenazolyl)-1,2,3-selenadiazoles VIa-VIf were prepared similarly (Table III).

(2-Methyl-4-thiazolyl)acetylene (VII, R = CH_3).

Compound VIg (460 mg, 2 mmoles) was heated at 145° for 5 minutes and distilled to give 123 mg (50%) of VII (R = CH_3), bp 144-145° (30 mm Hg); ir: 3300 (acetylene C-H), 2250 cm^{-1} (C≡C); nmr (deuteriochloroform): 7.36 (s, 1H, H_5), 3.1 (s, 1H, HC≡C) and 2.66 ppm (s, 3H, CH_3); ms: m/e (%) 123 (M^+, 100), 82 (94), 32 (41).

Anal. Calcd. for C_6H_5NS: C, 58.54; H, 4.07; N, 11.38. Found: C, 58.67; H, 4.18; N, 11.24.

(2-Phenyl-4-thiazolyl)acetylene was prepared similarly in 60% yield, mp 83-85° (ether); ir: 3280 (acetylene C-H), 2300 cm^{-1} (C≡C); nmr (deuteriochloroform): 8.08 (m, 2H, aromatic), 7.30 (m, 4H, aromatic) and 3.10 (s, 1H, HC≡C); ms: m/e (%) 185 (M^+, 100), 82 (99), 57 (11), 38 (12) and 32 (29).

Anal. Calcd. for $C_{11}H_7NS$: C, 71.35; H, 3.78; N, 7.57. Found: C, 71.18; H, 3.64; N, 7.69.

cis-2,ω-(2-Methyl-4-thiazolyl)-1,4-diselenafulvene (VIII, R = CH_3).

To a solution of II (R = CH_3, 231 mg, 1 mmole) in ethanol (10 ml) two pellets of potassium hydroxide was added. After the evolution of gas was ceased the precipitate filtered and recrystallized from ethanol to give 141 mg (70%) of VIII (R = CH_3), mp 155-157°; nmr (deuteriochloroform): 7.70 (s, 1H, H_3), 7.03 (s, 2H, aromatic), 6.80 (s, 1H, Hω), 2.80 (s, 3H, CH_3) and 2.70 ppm (s, 3H, CH_3); ms: m/e (%) 406 (M^+ +2, 100), 404 (88), 402 (52), 283 (27), 281 (25), 279 (14), 242 (13), 203 (22), 123 (25), 82 (40) and 32 (48).

Anal. Calcd. for $C_{12}H_{10}N_2S_2Se_2$: C, 35.64; H, 2.48; N, 6.93. Found: C, 35.78; H, 2.53; N, 7.01.

Heating of compound VIII (R = CH_3) at 200° for 15 minutes caused isomerization to *trans* compound IX (R = CH_3), mp 203-205° (ethanol).

cis-2,ω-(2-Phenyl-4-thiazolyl)-1,4-diselenafulvene (VIII, R = C_6H_5).

This compound was prepared similarly in 80% yield, mp 160-162°; ms: m/e (%) 530 (M +2, 8), 528 (M^+, 8), 346 (23), 344 (53), 342 (47), 257 (29), 255 (100), 253 (55), 242 (29), 240 (26), 185 (69), 162 (23) and 82 (52).

Heating compound VIII (R = C_6H_5) at 200° for 15 minutes caused isomerization to *trans* compound IX (R = C_6H_5), mp 218-220°.

5-(2-Methyl-4-thiazolyl)-2-thioxo-1,3-thiaselenole (XI, R = CH_3).

To a stirred solution of compound II (R = CH_3, 2.3 g, 0.01 mole) in dioxane (50 ml), a solution of potassium hydroxide (0.56 g, 0.01 mole) in ethanol (10 ml) was added, whereupon the evolution of nitrogen ceases. Then, tetrahydrofuran (10 ml) and carbon disulfide (5 ml) were added and stirring was continued for 1 hour at room temperature. The solvent was evaporated under reduced pressure, water (100 ml) was added to the residue, and the mixture was extracted with chloroform. The extract was dried with sodium sulfate, filtered and evaporated. The residue was purified by preparative tlc on silica gel using chloroform-petroleum ether (30:70) as eluent. The desired compound was crystallized from carbon tetrachloride to give 1.39 g (50%) of XI, mp 142-144°; nmr (deuteriochloroform): 8.0 (s, 1H, H_4), 7.10 (s, 1H, H_5-thiazole), and 2.70 ppm (s, 3H, CH_3); ms: m/e (%): 279 (M^+ +1, 100), 277 (49), 203 (41), 201 (20), 162 (37), 160 (19), 118 (12), 117 (13), 112 (14), 82 (24), and 69 (12).

5-(2-Phenyl-4-thiazolyl)-2-thioxo-1,3-thiaselenole (XI, R = C_6H_5).

This compound was prepared similarly in 60% yield, mp 185-187° (chloroform): ms: m/e (%) 341 (M^+ +1, 17), 265 (21), 263 (13), 185 (11), 162 (27), 160 (12), 121 (28), 112 (27), 82 (100), 69 (74), 51 (36), 50 (24) and 45 (31).

Anal. Calcd. for $C_{12}H_7N_3Se$: C, 42.35; H, 2.06; N, 4.12. Found: C, 42.18; H, 2.01; N, 4.28.

Acknowledgment.

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REFERENCES AND NOTES

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