Selenium Heterocycles. XXXV (1). Synthesis and Pyrrolysis of Aryloxy-, Arylthio-, and Arylseleno-1,2,3-selenadiazoles

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A series of 4-substituted-5-arylthio-1,2,3-selenadiazoles, 4-substituted-5-arylseleno-1,2,3-selenadiazoles and 4-aryloxymethyl-1,2,3-selenadiazoles were synthesized. Pyrrolysis of these compounds afforded the corresponding acetylenes XI, XIII (X = S, Se) and XII, respectively. Oxidation of 4-substituted-5-arylthio-1,2,3-selenadiazoles (XIV) with *m*-chloroperbenzoic acid gave 4-substituted-5-arylsulfinyl-1,2,3-selenadiazoles (XV) and 4-substituted-5-arylsulfonyl-1,2,3-selenadiazoles (XVI).

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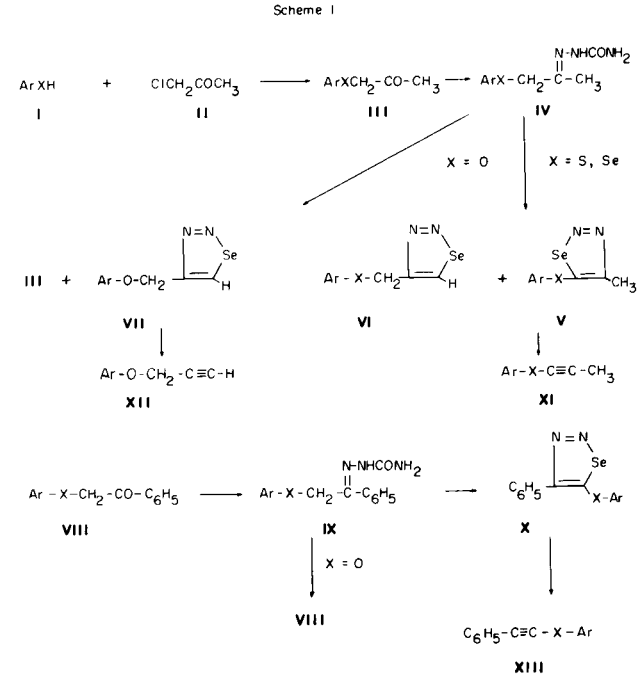
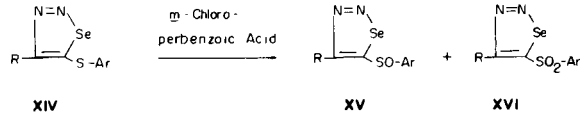
The synthesis of 1,2,3-selenadiazoles by selenium dioxide oxidation of aldehyde or ketone semicarbazones having and α-methyl or methylene group was previously reported (2-4). It was demonstrated that the direction of ring closure, when both α positions of semicarbazones are available for ring closure, depends on the effect the substituents have on the acidity of α hydrogens. Thus electron-attracting substituent, which increases the acidity of methylene hydrogen relative to the methyl group lead to the preferential ring closure on the methylene side (4). In continuation of the latter study, and in order to determine the effect of oxygen, sulfur and selenium on the direction of ring closure, a series of aryloxy-, arylthio-, and arylselenoacetone semicarbazones were prepared and selenium dioxide oxidation of these compounds were studied.

The required α-substituted-acetone semicarbazones (III) were prepared according to Scheme I.

Scheme I





Phenols, thiophenols and selenophenols were condensed with α-chloroacetone (II) to give the desired carbonyl compounds (III) (5,6). The reaction of phenylthioacetone semicarbazone (IV, Ar = C_6H_5, X = S) with selenium dioxide in acetic acid afforded 4-methyl-5-phenylthio-1,2,3-selenadiazole (V, Ar = C_6H_5, X = S) as a major product and 4-phenylthiomethyl-1,2,3-selenadiazole (VI, Ar = C_6H_5, X = S) as a minor product as determined by nmr. In the nmr spectrum of the product, in addition to the aromatic peak at 7.66-7.16, three peaks at 8.83, 4.60 and 2.66 ppm were observed. The peaks at 8.83 and 4.60 were assigned to compound VI (H_5 and CH_2, respectively) and the peak to 2.66 to compound V (methyl). The ratio of compound V (Ar = C_6H_5, X = S) to VI (Ar = C_6H_5, X = S) was 9:1 as determined by nmr. Similar result was observed for the selenium dioxide oxidation of the other α-arylthioacetone semicarbazones (IV, X = S) and α-arylselenoacetone semicarbazones (IV, X = Se). The above results demonstrates that sulfur and selenium direct the ring closure toward the methylene group. The reaction of α-aryloxyacetone semicarbazones (IV, X = O) with selenium dioxide in acetic acid gave in addition to the starting ketone III (X = O) as a major compound, exclusively 4-aryloxymethyl-1,2,3-selenadiazoles (VII). This demonstrates that in the selenium dioxide oxidation of compound IV (X = O) the cleavage is faster that ring formation. In addition, oxygen directs the ring closure toward the methyl group.

The reaction of α-arylthioacetophenone semicarbazones (IX, X = S) and α-arylselenoacetophenone semicarbazones (IX, X = Se) with selenium dioxide afforded 5-arylthio-4-phenyl-1,2,3-selenadiazoles (X, X = S) and 5-arylseleno-4-phenyl-1,2,3-selenadiazoles (X, X = Se) respectively. However, the reaction of α-aryloxyacetophenone semicarbazones (IX, X = O) with selenium dioxide in

Table I

Ar-X-CH_2-CO-R

Ar	R	X	Yield	Mp °C[a] or Bp °C/mm Hg	Formula	C% Calcd.	C% Found	H% Calcd.	H% Found
C_6H_5-	CH_3	O	90	120-122/20[b]	$C_9H_{10}O_2$	72.00	72.15	6.67	6.54
p-ClC_6H_4-	CH_3	O	65	140-142/20	$C_9H_9ClO_2$	58.54	58.46	4.88	4.95
p-$CH_3C_6H_4$-	CH_3	O	60	160-162/20	$C_{10}H_{12}O_2$	73.17	73.29	7.32	7.51
C_6H_5-	C_6H_3	O	50	175-178/4[c]	$C_{14}H_{12}O_2$	79.25	79.08	5.66	5.48
C_6H_5-	CH_3	S	70	32-34	$C_9H_{10}OS$	65.06	64.93	6.02	5.91
p-BrC_6H_4-	CH_3	S	75	54-55	C_9H_9BrOS	44.08	43.94	3.67	3.84
p-ClC_6H_4-	CH_3	S	75	56-57	C_9H_9ClOS	53.87	53.99	4.49	4.31
p-$CH_3C_6H_4$-	CH_3	S	70	178-180/20	$C_{10}H_{12}OS$	66.67	66.85	6.67	6.49
$C_6H_5CH_2$-	CH_3	S	65	53-54	$C_{10}H_{12}OS$	66.67	66.48	6.67	6.52
α-Naphthyl-	CH_3	S	70	225-230/20	$C_{13}H_{12}OS$	72.22	72.14	5.56	5.74
C_6H_5-	C_6H_5	S	90	52-54	$C_{14}H_{12}OS$	73.68	73.84	5.26	5.44
p-BrC_6H_4-	C_6H_5	S	80	82-84	$C_{14}H_{11}BrOS$	54.72	54.89	3.58	3.41
p-ClC_6H_4-	C_6H_5	S	80	80-82	$C_{14}H_{11}ClOS$	64.00	64.18	4.19	4.01
C_6H_5-	*p*-$CH_3OC_6H_4$-	S	70	87-88	$C_{15}H_{14}O_2S$	69.77	69.63	5.43	5.29
p-$CH_3OC_6H_4$-	*p*-$CH_3OC_6H_4$-	S	65	138-141	$C_{16}H_{16}O_3S$	66.67	66.83	5.56	5.73
C_6H_5-	CH_3	Se	70	124-126/4	$C_9H_{10}OSe$	50.70	50.58	4.69	4.82
p-BrC_6H_4-	CH_3	Se	75	56-58	C_9H_9BrOSe	36.99	37.12	3.08	2.91
p-ClC_6H_4-	CH_3	Se	75	60-62	C_9H_9ClOSe	43.64	43.82	3.64	3.51
C_6H_5-	C_6H_5	Se	80	53-55	$C_{14}H_{12}OSe$	61.09	60.92	4.36	4.19

(a) Unless otherwise mentioned the compound was crystallized from ether-petroleum ether. (b) Reference (5), bp 117-120°/19 mm. (c) Reference (8), bp 187°/8 mm.

acetic acid gave only starting materials.

Pyrrolysis of compounds V, VII and X yielded the corresponding acetylenes XI, XII, and XIII repectively.

Oxidation of 4-substituted-5-arylthio-1,2,3-selenadiazoles (XIV) with *m*-chloroperbenzoic acid gave 4-substituted-5-arylsulfinyl-1,2,3-selenadiazoles (XV) as the major product and 4-substituted-5-arylsulfonyl-1,2,3-selenadiazoles (XVI) (7) as the minor product. The structure of compound XV was confirmed through the further oxidation with *m*-chloroperbenzoic acid which gave XVI.

The structure of all compounds was confirmed by analytical and spectroscopic methods.

The physical constants of all compounds prepared are summarized in Tables I-IV.

EXPERIMENTAL

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. 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.

Arylthioacetones (III, X = S).

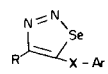
These compounds were prepared according to the literature (6) (See Table I).

Arylselenoacetones (III, X = Se) were prepared similarly (See Table I).

Aryloxyacetones (III, X = O).

These compounds were prepared according to the literature (5) (See Table I).

Table II



Ar	R	X	Yield (%)	Mp °C (a)	Formula	C% Calcd	C% Found	H% Calcd.	H% Found	N% Calcd.	N% Found
C_6H_5-	CH_3	S	70	32-34	$C_9H_8N_2SSe$	42.35	42.19	3.14	3.02	10.98	11.13
p-BrC_6H_4-	CH_3	S	75	45-47	$C_9H_7BrN_2SSe$	32.34	32.51	2.10	1.95	8.36	8.16
p-ClC_6H_4-	CH_3	S	70	48-49	$C_9H_7ClN_2SSe$	37.31	37.14	2.42	2.29	9.67	9.85
p-$CH_3C_6H_4$-	CH_3	S	65	oil	$C_{10}H_{10}N_2SSe$	44.61	44.78	3.72	3.59	10.41	10.25
$C_6H_5CH_2$-	CH_3	S	75	oil	$C_{10}H_{10}N_2SSe$	44.61	44.80	3.72	3.86	10.41	10.58
α-Naphthyl-	CH_3	S	70	103-105	$C_{13}H_{10}N_2SSe$	51.15	51.06	3.28	3.11	9.18	9.03
C_6H_5-	CH_3	S	50	34-35	$C_9H_8N_2Se_2$	35.76	35.94	2.65	2.84	9.27	9.08
p-BrC_6H_4-	CH_3	Se	50	48-49	$C_9H_7BrN_2Se_2$	28.35	28.49	1.84	1.98	7.35	7.47
p-ClC_6H_4-	CH_3	Se	55	50-51	$C_9H_7ClN_2Se_2$	32.10	31.94	2.08	2.26	8.32	8.51
α-Naphthyl-	CH_3	Se	50	106-107	$C_{13}H_{10}N_2Se_2$	44.32	44.51	2.84	2.95	7.95	8.18
C_6H_5-	C_6H_5	S	65	70-72	$C_{14}H_{10}N_2SSe$	53.00	53.15	3.15	3.29	8.83	8.96
p-ClC_6H_4-	C_6H_5	S	65	92-94	$C_{14}H_9ClN_2SSe$	47.80	47.67	2.56	2.39	7.97	8.01
p-BrC_6H_4-	C_6H_5	S	70	108-110	$C_{14}H_9BrN_2SSe$	42.42	42.61	2.27	2.19	7.07	7.19
C_6H_5-	*p*-$CH_3OC_6H_4$-	S	60	94-95	$C_{15}H_{12}N_2OSSe$	51.87	51.98	3.46	3.65	8.07	8.21
p-$CH_3OC_6H_4$-	*p*-$CH_3OC_6H_4$-	S	40	98-100	$C_{16}H_{14}N_2O_2SSe$	50.93	51.12	3.71	3.90	7.43	7.58
C_6H_5-	C_6H_5	Se	45	71-73	$C_{14}H_{10}N_2Se_2$	46.15	46.02	2.75	2.93	7.69	7.83

(a) All compounds were crystallized from ether-petroleum ether.

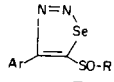
Table III

Ar-X-C≡C-R

Ar	R	X	Yield (%)	Bp °C/mm Hg[a] (a)	Formula	C% Calcd.	C% Found	H% Calcd.	H% Found
C_6H_5-	CH_3	S	90	115-116/20 (b)	C_9H_8S	72.97	73.14	5.41	5.60
p-BrC_6H_4-	CH_3	S	85	120-122	C_9H_7BrS	47.58	47.74	3.08	3.19
p-ClC_6H_4-	CH_3	S	85	112-114	C_9H_7ClS	59.18	59.06	3.84	3.98
p-$CH_3C_6H_4$-	CH_3	S	87	110-112	$C_{10}H_{10}S$	74.07	73.92	6.17	6.08
$C_6H_5CH_2$-	CH_3	S	89	123-124	$C_{10}H_{10}S$	74.07	74.24	6.17	6.35
C_6H_5-	CH_3	Se	80	81-83/1 (c)	C_9H_8Se	55.38	55.19	4.10	4.25
p-BrC_6H_4-	CH_3	Se	75	124-126	C_9H_7BrSe	39.42	39.27	2.55	2.73
p-ClC_6H_4-	CH_3	Se	80	116-118	C_9H_7ClSe	47.06	46.95	3.07	3.15
C_6H_5-	C_6H_5	S	85	135-140 (d)	$C_{14}H_{10}S$	80.00	80.19	4.76	4.59
p-BrC_6H_4-	C_6H_5	S	80	165-170	$C_{14}H_9BrS$	58.13	58.27	3.11	3.26
p-ClC_6H_4-	C_6H_5	S	80	155-158	$C_{14}H_9ClS$	68.71	68.90	3.68	3.79
C_6H_5-	*p*-$CH_3OC_6H_4$-	S	75	172-175	$C_{15}H_{12}OS$	75.00	75.19	5.00	4.86
C_6H_5-	C_6H_5-	Se	60	143-145	$C_{14}H_{10}Se$	65.37	65.19	3.89	3.98

(a) Unless otherwise mentioned the compound was distilled at 4 mm Hg. (b) Reference (9) bp 78-81/0.75 mm. (c) Reference (10) bp 77°/0.5 mm. (d) Reference (11) bp 155-170/2.5 mm.

Table IV



Ar	R	Yield (%)	Mp °C (a)	Formula	C% Calcd.	C% Found	H% Calcd	H% Found	N% Calcd.	N% Found
C_6H_5-	CH_3	35	oil	$C_9H_8N_2OSSe$	39.85	40.03	2.95	3.14	10.33	10.52
p-BrC_6H_4-	CH_3	40	103-105	$C_9H_7BrN_2OSSe$	30.86	30.69	2.00	1.87	8.00	8.18
p-ClC_6H_4-	CH_3	40	106-108	$C_9H_7ClN_2OSSe$	35.35	35.18	2.29	2.14	9.17	9.04
p-$CH_3C_6H_4$-	CH_3	40	oil	$C_{10}H_{10}N_2OSSe$	42.11	42.30	3.51	3.35	9.82	9.65
$C_6H_5CH_2$-	CH_3	38	98-100	$C_{10}H_{10}N_2OSSe$	42.11	42.28	3.51	3.68	9.82	10.01
a-Naphthyl-	CH_3	35	102-103	$C_{13}H_{10}N_2OSSe$	48.60	48.76	3.12	3.01	8.72	8.65
C_6H_5-	C_6H_5	40	114-115	$C_{14}H_{10}N_2OSSe$	50.45	50.63	3.00	2.86	8.41	8.39
p-BrC_6H_4-	C_6H_5	45	99-101	$C_{14}H_9BrN_2OSSe$	40.78	40.93	2.18	2.04	6.80	6.65
p-ClC_6H_4-	C_6H_3	45	103-105	$C_{14}H_9ClN_2OSSe$	45.71	45.83	2.45	2.63	7.62	7.81
C_6H_5-	$pCH_3OC_6H_4$-	35	99-100	$C_{15}H_{12}N_2O_2SSe$	49.59	49.72	3.31	3.15	7.71	7.56
p-$CH_3OC_6H_4$-	*p*-$CH_3OC_6H_4$-	30	145-147	$C_{16}H_{14}N_2O_3SSe$	48.85	48.67	3.56	3.63	7.12	7.31

(a) All compounds were crystallized from ether-petroleum ether.

4-Methyl-5-phenylthio-1,2,3-selenadiazole (V, Ar = C_6H_5, X = S).

To α-phenylthioacetone semicarbazone (2.33 g, 0.01 mole) in 25 ml of acetic acid selenium dioxide (1.1 g, 0.01 mole) was added. The mixture was gently heated until gas evolution ceased. The dark mixture was treated with charcoal, filtered, diluted with water and extracted with chlorofrom. The organic layer was washed with aqueous sodium bicarbonate solution, dried, filtered and evaporated. The residue was purified by tlc (silica gel, chloroform) to give a mixture of V (Ar = C_6H_5, X = S) and 4-phenylthiomethyl-1,2,3-selenadiazole (VI, Ar = C_6H_5, X = S) in ratio of 9:1; nmr (deuteriochloroform): 8.83 (s, H_5 of VI), 7.66-7.16 (m, 5H, aromatic), 4.60 (s, CH_2 of VI) and 2.66 ppm (s, CH_3 of V). The mixture was crystallized from ether-petroleum ether to give 1.78 g. (70%) of V (Ar = C_6H_5, X = S), mp 32-34°; ms: m/e (%): 256 (M^+, 43), 228 (M-28, 30), 148 (100), 115 (93), 109 (70), 77 (60), 69 (52), 65 (73), 51 (80) and 39 (53).

Other selenadiazoles (V and X) were prepared similarly (See Table II).

4-Phenoxymethyl-1,2,3-selenadiazole (VII, Ar = C_6H_5).

α-Phenoxyacetone semicarbazone (2.07 g, 0.01 mole) was treated with selenium dioxide as explained above and purified by tlc (silica gel, chloroform). The faster moving fraction was *a*-phenoxyacetone (0.97 g, 65%). The slow moving fraction was crystallized from ether to give 0.6 g (25%) of VII (Ar = C_6H_5), mp 98-100°; nmr (deuteriochloroform): 9.27 (s, 1H, H_5), 7.60-6.70 (m, 5H, aromatic) and 5.60 ppm (s, 2H, CH_2); ms: m/e (%) 240 (M^+, 55), 212 (8), 132 (37), 131 (100), 119 (98), 94 (99), 93 (50), 77 (59), 65 (58), 55 (34), 51 (47) and 39 (78).

Anal. Calcd. for $C_9H_8N_2OSe$: C, 45.19; H, 3.35; N, 11.72. Found: C, 45.03; H, 3.21; N, 11.61.

4-*p*-Tolyoxymethyl-1,2,3-selenadiazole (VII), Ar = *p*-$CH_3C_6H_4$-).

This compound was prepared similarly in 20% yield, mp 87-89° (petroleum ether); nmr (deuteriochloroform): 9.37 (s, 1H, H_5), 7.03 (ABq, 4H, aromatic), 5.67 (s, 2H, CH_2) and 2.30 ppm (s, 3H, CH_3).

Anal. Calcd. for $C_{10}H_{10}N_2OSe$: C, 47.43; H, 3.95; N, 11.07. Found: C, 47.61; H, 3.82; N, 10.98.

4-*p*-Chlorophenylmethoxy-1,2,3-selenadiazole (VII, Ar = *p*-ClC_6H_4-).

This compound was prepared similarly in 25% yield, mp 99-100° (petroleum ether).

Anal. Calcd. for $C_9H_7ClN_2OSe$: C, 39.49; H, 2.56; N, 10.24. Found: C, 39.65; H, 2.67; N, 10.38.

Phenyl 1-Propynyl Sulfide (XI, Ar = C_6H_5, X = S).

Compound V (Ar = C_6H_5, X = S, 2.55 g, 0.01 mole) was heated at 180° for 5 minutes. The product was distilled under reduced pressure to give 1.33 g (90%) of XI, bp 115-116 ° (20 mm Hg); nmr (CCl_4): 7.50-7.03 (m, 5H, aromatic) and 2.11 ppm (s, 3H, CH_3).

Other acetylenes (XI and XIII) were prepared similarly (See Table III).

Phenyl 2-Propynyl Ether (XII, Ar = C_6H_5).

Compound VII (Ar = C_6H_5, 2.39 g, 0.01 mole) was heated at 120° for 5 minutes. The product was distilled under reduced pressure to give 1 g. (76%) of XII (Ar = C_6H_5), bp 98-99° (20 mm Hg) [reference (10), bp 102° (30 mm Hg)].

Anal. Calcd. for C_9H_8O: C, 81.82; H, 6.06. Found: C, 82.01; H, 5.95.

p-Chlorophenyl 2-Propynyl Ether (XII, Ar = *p*-ClC_6H_4-).

This compound was prepared similarly in 75% yield, bp 88-89° (4 mm Hg).

Anal. Calcd. for C_9H_7ClO: C, 64.86; H, 4.20. Found: C, 64.97; H, 4.35.

p-Tolyl 2-Propynyl Ether (XII, Ar = *p*-$CH_3C_6H_4$-).

This compound was prepared similarly in 70% yield, bp 85-86° (4 mm Hg) [reference (12), bp 83-84° (3 mm Hg)].

Anal. Calcd. for $C_{10}H_{10}O$: C, 82.19; H, 6.85. Found: C, 82.04; H, 7.02.

Oxidation of 4-Methyl-5-Phenylthio-1,2,3-selenadiazole (XIV, R = CH_3, Ar = C_6H_5).

To a stirring solution of XIV (2.55 g, 0.01 mole) in 50 ml of ether a solution of *m*-chloroperbenzoic acid (85% pure, 3.03 g, 0.015 mole) in 50 ml of ether was added dropwise. After the addition was complete, stirring was continued for 1 hour. The solvent was evaporated and the residue was purified tlc (silica gel, chloroform). The faster moving fraction was crystallized from acetone-water to give 0.71 g (25%) of XVI (R = CH_3, Ar = C_6H_5), mp 76-78°, mixed melting point with an authentic sample (7) 76-78°. The slow moving fraction was an oil (0.95 g, 35%; XV, R = CH_3, Ar = C_6H_5); ms: m/e (%) 244 (M^+-28, 5), 201 (M-$C_2H_2N_2O$, 30), 149 (14), 121 (13), 119 (24), 116 (36), 115 (35), 105 (16), 97 (40), 93 (30), 87 (13), 85 (67), 83 (100), 77 (87), 71 (15), 59 (61) and 51 (64).

Anal. Calcd. for $C_9H_8N_2OSSe$: C, 39.85; H, 2.95; N, 10.33. Found: C, 40.03; H, 3.14; N, 10.52.

Other 4-substituted-5-arylsulfinyl-1,2,3-selenadiazoles (XV) were prepared similarly (See Table IV).

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