Selenium Heterocycles. V (1). Synthesis of Substituted *as*-Triazine-3-selenones and 6-Substituted-7*H*-selenazolo[3,2-*b*]-2,3-dihydro-1,2,4-triazine-3,7-diones.

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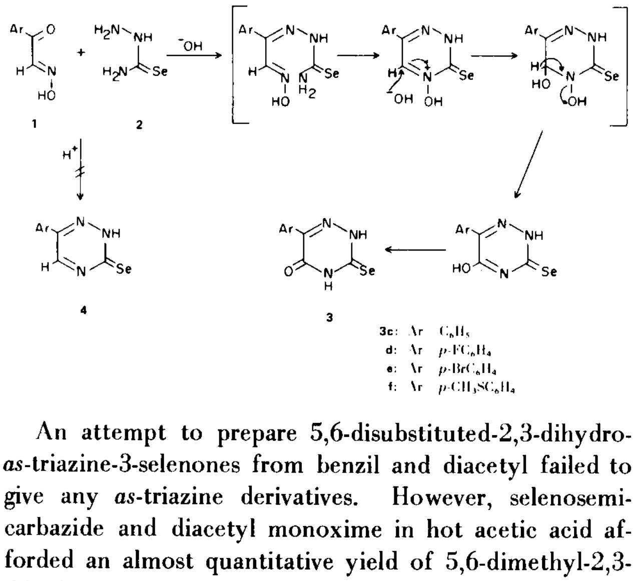
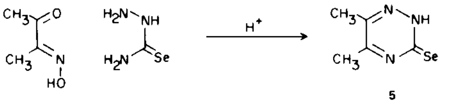
Recently we reported that substituted glyoxaldoxime semicarbazones cyclize in alkaline medium giving 6-substituted-2,3,4,5-tetrahydro-*as*-triazine-3,5-diones (2,3). Substituted glyoxaldoxime and thiosemicarbazide in alkaline medium afforded 6-substituted-2,3,4,5-tetrahydro-*as*-triazine-5-one-3-thiones (4). Both reactions, conducted in acid medium, led to the formation of 6-substituted-2,3-dihydro-*as*-triazine-3-ones and 6-substituted-2,3-dihydro-*as*-triazine-3-thiones, respectively (4,5).

The present work reports the synthesis and the chemistry of *as*-triazine-3-selenones which is part of a program dealing with the comparative chemistry of semicarbazide, thiosemicarbazide and selenosemicarbazide.

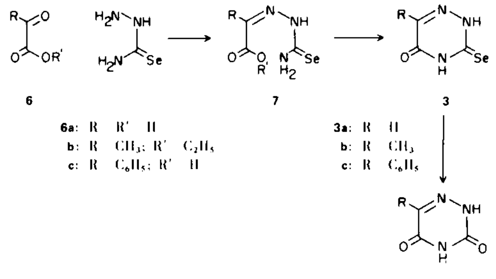
Reaction of selenosemicarbazide (**2**) and substituted phenylglyoxaldoximes (**1**) in boiling aqueous sodium carbonate solution afforded 6-aryl-2,3,4,5-tetrahydro-*as*-triazine-5-one-3-selenones (**3**). The same reaction conducted in acid medium failed to give 6-substituted-2,3-dihydro-*as*-triazine-3-selenones (**4**). In fact, selenosemicarbazide was decomposed in boiling dilute hydrochloric acid and black selenium was deposited during the reaction.



An attempt to prepare 5,6-disubstituted-2,3-dihydro-*as*-triazine-3-selenones from benzil and diacetyl failed to give any *as*-triazine derivatives. However, selenosemicarbazide and diacetyl monoxime in hot acetic acid afforded an almost quantitative yield of 5,6-dimethyl-2,3-dihydro-*as*-triazine-3-selenone (**5**).



In order to ascertain the structure of the new *as*-triazines, some of them were also prepared through an independent route by interaction of the α-keto acids (**6a,c**), or the α-keto ester (**6b**), with selenosemicarbazide giving the corresponding selenosemicarbazones (**7**). These were cyclized in alkaline medium to give the *as*-triazine derivatives (**3**). Further confirmation of the structure was obtained by alkaline potassium permanganate oxidation of **3c** to 6-phenyl-2,3,4,5-tetrahydro-*as*-triazine-3,5-dione.

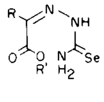


The physical data of selenosemicarbazones (**7**) are summarized in Table I.

The physical properties of *as*-triazine-3-selenones are listed in Table II.

In order to prepare 6-substituted-7*H*-selenazolo[3,2-*b*]-2,3-dihydro-1,2,4-triazine-3,7-diones (**9b,c**), 6-substituted 2,3,4,5-tetrahydro-*as*-triazine-5-one-3-selenones (**3**) were condensed with bromoacetic acid in sodium ethoxide-ethanol solution. The compounds obtained by this method proved to be 3-[carboxymethylseleno]-6-substituted-2,5-dihydro-*as*-triazine-5-ones (**8b,c**), rather than the expected bicyclic compounds **9**. To determine whether this effect was due to selenium, we repeated the experiment on its sulfur analogue. The compound obtained was the acid **8a** rather than the bicyclic compound **9a** reported previously (6). Cyclization attempted with thionyl chloride, phosphorus oxychloride or pyridine-acetic anhydride did

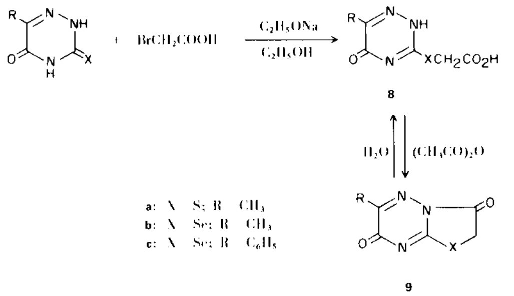
TABLE I



Compound	R	R'	M.p. °C	Yield %	Formula	C % Calcd.	C % Found	H % Calcd.	H % Found	N % Calcd.	N % Found
7a	H	H	182-183 (a)	85	$C_3H_5N_3O_2Se$	18.55	18.70	2.57	2.62	21.64	21.52
7b	CH_3	C_2H_5	135-137 (b)	90	$C_6H_{11}N_3O_2Se$	30.50	30.44	4.66	4.66	17.79	17.68
7c	C_6H_5	H	163-164 (b)	95	$C_9H_9N_3O_2Se$	40.00	39.89	3.33	3.32	15.55	15.61

(a) Crystallized from water. (b) Crystallized from ethanol-water.

not give satisfactory results. However, the acids **8** were successfully cyclized with acetic anhydride. Both sulfur and selenium bicyclic compounds **9a-c** were hydrolyzed in boiling water, yielding the starting acids **8**. Infrared spectra of sulfur and selenium analogues were very similar. Nmr spectra of bicyclic compounds **9** were in good agreement with their structures.



EXPERIMENTAL (7)

6-Substituted-2,3,4,5-tetrahydro-*as*-triazine-5-one-3-selenones (**3**).

Method A.

A solution of 2 mmoles of the appropriate arylglyoxaldoxime (**1**) (2) and 0.276 g. (2 mmoles) of selenosemicarbazide (**2**) (8) and 0.318 g. (3 mmoles) of sodium carbonate in 8 ml. of water was refluxed for 6 hours. The reaction mixture, after decolourizing with charcoal, was acidified with acetic acid and the precipitate was crystallized from the appropriate solvent (see Table II).

Method B.

To a solution of glyoxylic acid (0.01 mole) (**6a**) [or ethyl pyruvate (**6b**), or phenylglyoxylic acid (**6c**)] in water or ethanol was added a hot solution of 0.138 g. (0.01 mole) of selenosemicarbazide (**2**) in water. After 1/2 hour at room temperature, the precipitate was crystallized from the appropriate solvent (see Table I). The selenosemicarbazones (**7a-c**) were suspended in water and the *p*H of the mixture was adjusted to 12 (sodium hydroxide) and refluxed for 1/2 hour. During the course of the reaction the *p*H was readjusted to 12. After cooling, the reaction mixture was acidified with acetic acid and crystallized from the appropriate solvent (see Table II).

5,6-Dimethyl-2,3-dihydro-*as*-triazine-3-selenone (**5**).

A solution of 1 g. (0.01 mole) of diacetyl monoxime in 3 ml. of water was added to a hot solution of 1.34 g. (0.01 mole) of selenosemicarbazide (**2**) in 25 ml. of water. Acetic acid (3 ml.) was added to the reaction mixture which was then refluxed for 1/2 hour. The precipitate was filtered, washed with water and dried in an oven to give 1.8 g. (96%) of **5**, m.p. 203-204° dec.; m/e 188. The ir spectrum of **5** was very similar to its sulfur analogue (4).

Anal. Calcd. for $C_5H_7N_3Se$: C, 31.91; H, 3.72; N, 22.34. Found: C, 32.02; H, 3.79; N, 22.21.

6-Phenyl-7*H*-selenazolo[3,2-*b*]-2,3-dihydro-1,2,4-triazine-3,4-dione (**9c**).

To a hot solution of 0.02 mole of sodium ethoxide in 100 ml. of ethanol was added 2.53 g. (0.01 mole) of 6-phenyl-2,3,4,5-tetrahydro-*as*-triazine-5-one-3-selenone (**3c**) and 1.39 g. (0.01 mole) of bromoacetic acid. The refluxing was continued for 1/2 hour. The precipitate was filtered, dissolved in water and reprecipitated with concentrated hydrobromic acid to give 2.7 g. (87%) of 3-(carboxymethylseleno)-6-phenyl-2,5-dihydro-*as*-triazine-5-one (**8c**), m.p. 160-162° (acetic acid); ν max cm^{-1}, 1690-1680 (C=O of carboxylic acid and cyclic amide), 1555, 1485, 1430, 1348, 1265 (carboxylic acid), 1180, 1010, 805, 750, 715, 685.

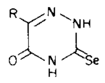
Anal. Calcd. for $C_{11}H_9N_3O_3Se$: C, 42.58; H, 2.90; N, 13.54. Found: C, 42.59; H, 2.86; N, 13.70.

Cyclization of **8c** was achieved by boiling 0.3 g. (0.01 mole) of **8c** in 3 ml. of acetic anhydride until complete dissolution. The excess of acetic anhydride was removed under reduced pressure. The residue was crystallized from ethyl acetate to give 0.28 g. (96%) of **9c**, m.p. 183-184°; m/e 292; uv max nm (log ϵ) 250 (4.17); 274 (4.28); ν max cm^{-1}, 1740 (five membered cyclic amide), 1645 (six membered conjugated cyclic amide), 1524, 1493, 1471, 1361, 1316, 1290, 1190, 1176, 1031, 1020, 840, 809, 752, 690; nmr (dimethylsulfoxide), τ 5.70 (s, 2, CH_2), 1.9-2.7 (m, 5, C_6H_5).

Anal. Calcd. for $C_{11}H_7N_3O_2Se$: C, 45.20; H, 2.39; N, 14.38. Found: C, 45.20; H, 2.45; N, 14.33.

The bicyclic compound **9c** was hydrolyzed on boiling with aqueous acetone and afforded the starting acid **8c**.

TABLE II



Compound (a)	R	M.p. °C	Yield %	Formula	C %		H %		N %		λ max (b) (nm)	log ε
					Calcd.	Found	Calcd.	Found	Calcd.	Found		
3a	H	200-204 (c)	60	$C_3H_3N_3OSe$	20.45	20.55	1.70	1.67	23.86	23.90	212 300	4.16 4.39
3b	CH_3	208-209 (c)	90	$C_4H_5N_3OSe$	25.26	25.24	2.63	2.60	22.10	22.18	212 300	4.12 4.13
3c	C_6H_5	235-236 (c)	79	$C_9H_7N_3OSe$	42.85	42.79	2.77	2.81	16.66	16.62	224 305	3.90 4.14
3d	*p*-FC_6H_4	220-222 (d)	79	$C_9H_6FN_3OSe$	40.00	40.04	2.22	2.20	15.55	15.61	224 306	4.04 4.27
3e	*p*-BrC_6H_4	235-237 (e)	69	$C_9H_6BrN_3OSe$	32.62	32.50	1.81	1.88	12.68	12.61	224 307	4.04 4.34
3f	*p*-$CH_3SC_6H_4$	185-190 (e)	82	$C_{10}H_9N_3OSSe$	40.26	40.27	3.02	2.99	14.09	13.99	224 290	4.04 4.30

(a) Compounds **3a-3c** were prepared by Method B; compounds **3c-3f** were prepared by Method A. (b) In ethanol. (c) Crystallized from ethanol. (d) Crystallized from acetic acid-water. (e) Crystallized from ethanol-water.

6-Methyl-7*H*-selenazolo[3,2-*b*]-2,3-dihydro-1,2,4-triazine-3,7-dione (**9b**).

To a hot solution of 0.02 mole of sodium ethoxide in 100 ml. of ethanol and 1.90 g. (0.01 mole) of 6-methyl-2,3,4,5-tetrahydro-*as*-triazine-5-one-3-selenone (**3b**) was added 1.39 g. (0.01 mole) of bromoacetic acid. After 1/2 hour refluxing, the solvent was evaporated and the residue was dissolved in water and acidified with hydrobromic acid. The precipitate was crystallized from water to give 0.99 g. (40%) of **8b**, m.p. 145-150°; ν max cm^{-1}, 1680 (C=O), 1285 (carboxylic acid).

Anal. Calcd. for $C_6H_7N_3O_3Se$: C, 29.03; H, 2.82; N, 16.93. Found: C, 28.98; H, 2.85; N, 16.90.

Cyclization of **8b** was effected by boiling of 0.248 g. (1 mmole) of carboxylic acid **8b** in 3 ml. of acetic anhydride until complete dissolution. The excess of acetic anhydride was removed under reduced pressure and the residue was crystallized from ethyl acetate to give 1.61 g. (70%) of **9b**, m.p. 175-180°; m/e 230; uv max nm (log ϵ) 243 (4.16) (dioxane); ν max cm^{-1}, 1755 (C=O of five membered cyclic amide) and 1670 (six membered conjugated cyclic amide).

Anal. Calcd. for $C_6H_5N_3O_2Se$: C, 31.30; H, 2.17; N, 18.26. Found: C, 31.25; H, 2.21; N, 18.29.

The bicyclic compound **9b** was also hydrolyzed to the starting acid **8b** in boiling aqueous acetone.

3-(Carboxymethylthio)-6-methyl-2,5-dihydro-*as*-triazine-5-one (**8a**).

This compound was prepared similarly to its seleno analogue, m.p. 170-175°; ν max cm^{-1}, 1725 (C=O), 1258 (carboxylic acid).

Anal. Calcd. for $C_6H_7N_3O_3S$: C, 35.82; H, 3.48; N, 20.89. Found: C, 35.75; H, 3.51; N, 21.06.

Cyclization of acid **8a** according to the method described above gives 6-methyl-7*H*-thiazolo[3,2-*b*]-2,3-dihydro-1,2,4-triazine-3,7-dione (**9a**), m.p. 174-175° (lit. (6) 175°); m/e 183; uv max nm (log ϵ) 238 (5.2) (dioxane); ν max cm^{-1}, 1755 (C=O of five membered cyclic amide), 1660 (six membered conjugated cyclic amide).

Anal. Calcd. for $C_6H_5N_3O_2S$: C, 39.34; H, 2.73; N, 22.95. Found: C, 39.29; H, 2.80; N, 22.89.

The bicyclic compound **9a** was hydrolyzed on boiling with aqueous acetone and afforded the starting acid **8a**.

6-Phenyl-2,3,4,5-tetrahydro-*as*-triazine-3,5-dione.

A solution of 0.5 g. of **3c** in 20 ml. of 5% aqueous sodium hydroxide was treated at room temperature with a saturated potassium permanganate solution until the pink color persisted. The excess of potassium permanganate was decomposed by alcohol and filtered. The solution was acidified to give a white precipitate which was recrystallized from dilute alcohol to give 0.34 g. (92%), m.p. 262° (lit. (2) 262°).

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(7) Melting points were determined on a Kofler hot stage microscope and were uncorrected. The infrared spectra were obtained using a Leitz model III spectrograph (potassium bromide discs). The nmr spectra were recorded on a Varian A60A instrument. The mass spectra were recorded on a Varian Mat 111 instrument. The uv spectra were taken with a Unicam Sp. 800 spectrophotometer.

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