Selenium Heterocycles. XV. (1) Reaction of 2-Aminoselenazoles and 2-Amino-1,3,4-selenadiazoles with Acetylenic Compounds

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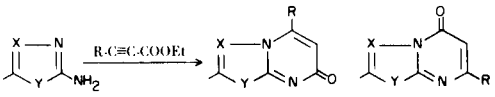
2-Aminoselenazoles with ethyl propiolate or dimethyl acetylenedicarboxylate gave 7*H*-selenazolo[3,2-*a*]pyrimidin-7-ones. 2-Amino-1,3,4-selenadiazoles with dimethyl acetylenedicarboxylate gave 7*H*-1,3,4-selenadiazolo[3,2-*a*]pyrimidin-7-ones; with ethyl propiolate the reaction took an unusual path and 2-carbethoxy-5*H*-selenazolo[3,2-*a*]pyrimidin-5-one was isolated. The assignment of the structures were supported by spectra analysis.

Previously, synthesis of 5-substituted-2-amino-1,3,4-selenadiazoles and their reactions with α-haloketone were reported (2). In this work reactions of this hetercycle and 4-substituted-2-aminoselenazoles with ethyl propiolate and dimethyl acetylenedicarboxylate are reported.

In recent years reaction of different nitrogen heterocycles having an α-amino group with acetylenic compounds have been studied (3-8). Generally speaking two alternative structures for the products are possible (See Scheme I).

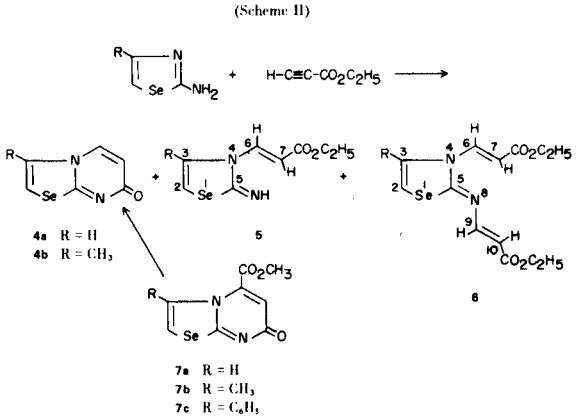
(Scheme I)



Reaction of 2-aminothiazoles and 2-aminobenzothiazoles with ethyl propiolate gives 7*H*-thiazolo[3,2-*a*]pyrimidin-7-ones (**2**) and 2*H*-pyrimido[2,1-*b*]benzothiazol-2-one respectively, and not the alternative isomeric 5*H*-thiazolo[3,2-*a*]pyrimidin-5-one (**3**) and 4*H*-pyrimido[2,1-*b*]benzothiazole-4-one (3,4). Similar results were observed for 2-aminobenzoxazole and 2-aminobenzimidazole (5). However, Henklein, *et al.*, (6) reported that the reaction of 2-amino-1,3,4-oxadiazoles with acetylenic compounds afforded only 5*H*-1,3,4-oxadiazolo[3,2-*a*]pyrimidin-5-ones (**3**); in the case of 3-aminobenzisoxazole a mixture of the two isomers was obtained (7).

We have found that the major products from the reaction of 4-substituted-2-aminoselenazoles with ethyl propiolate and dimethyl acetylenedicarboxylate are substituted-7*H*-selenazolo[3,2-*a*]pyrimidin-7-ones (**2**), and not the alternative isomeric substituted-5*H*-selenazolo[3,2-*a*]-pyrimidin-5-ones (3). Distinction between the alternative

(Scheme II)

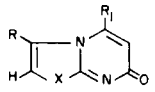


structures was based on ir, uv, and nmr data.

In the reaction of 2-aminoselenazole with ethyl propiolate in addition to compound **4a** (50% yield), compounds **5** and **6** were also isolated; **4** is probably formed through the *cis* isomer of **5** (See Scheme II).

Allen, *et al.*, (8) reported that the uv spectra of the two series (5-ones and 7-ones) are quite different: in the 7-one series the c-band (*ca.* 300 nm) either does not exist or has a small intensity, while in the case of 5-one series this band is very intense and appears at higher wave lengths (4). Similarly, it is reported that the ir spectra of the two series are quite different (4). The amide bands of 7-ones appear below 1655 cm^{-1}, while the same absorption for the 5-ones are above 1655 cm^{-1}. As can be seen in Table I, the ir and uv spectra of compound **4** are in agreement with the 7-one isomer. In addition, the ir and uv of compound **4** were similar to 7*H*-thiazolo[3,2-*a*]pyrimidin-7-one and quite different from its isomer 5*H*-thiazolo[3,2-*a*]-pyrimidin-5-one (3). The *trans* configuration of compound **5**, 1:1 adduct, and compound **6**, 1:2 adduct, were con-

(Table I)



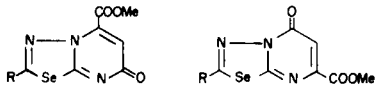
X	R	R_1	MP, °C	Ir (cm^{-1}, amide)	Uv λ max (ethanol), (log ε) λ_a (nm)	λ_b (nm)	λ_c (nm)
Se	H	H	276-278 (a)	1635	215 (3.22)	283 (4.04), 235 (4.18)	
Se	CH_3	H	298-300 (a)	1635	218 (4.09)	287 (4.04), 238 (4.17)	
Se	H	$COOCH_3$	157-158 (b)	1640	217 (4.01)	293 (3.99), 253 (4.15)	
Se	H	COOH	195-196 (c)	1630	218 (4.19)	283 (4.03), 237 (4.17)	344 (3.49)
Se	Ph	$COOCH_3$	192-193 (b)	1640	215 (4.16)	246 (4.24)	300 (3.77)
S	H	H	270-272 (a)	1634	213 (4.26)	271 (4.12), 230 (4.08) (3)	
S	H	$COOCH_3$	172-174 (d)	1638	210 (4.17)	285 (4.04), 242 (4.38)	

(a) Crystallized from DMSO. (b) Crystallized from DMSO-ethyl acetete. (c) Crystallized from water. (d) Crystallized from ethanol.

firmed by nmr.

The reaction of substituted 2-aminoselenazoles with dimethyl acetylenedicarboxylate gave only the 7-one isomers **7**. The structure of these compounds were established by conversion to **4**. In addition, the nmr spectrum of 3-phenyl-5-carbomethoxy-7*H*-selenazolo[3,2-*a*]pyrimidin-7-one (**7c**) was in agreement with this assignment. In this case, the ester group appeared at 2.93 ppm, showing the shielding of the ester by phenyl group at position 3. The physical properties of the compounds prepared are summarized in Table I.

The reaction of 2-amino-1,3,4-selenadiazoles with dimethyl acetylenedicarboxylate gave only one of the two possible isomers **8** or **9**. To establish the structure, we attempted to prepare one of the isomers by an independent

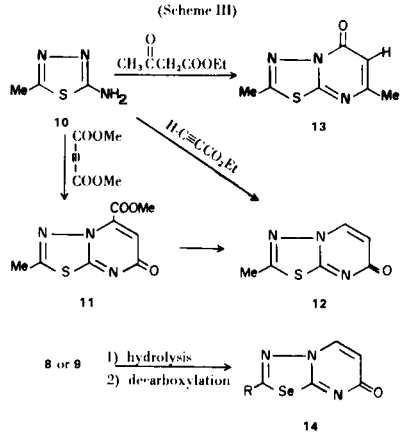


8 **9**

method. The reaction of 2-amino-1,3,4-selenadiazole with ethyl acetoacetate in refluxing acetic acid was investigated. However, the substance decomposed under the reaction conditions and selenium was released. The alternative method for establishing the structure was to prepare the thia-analogs of **8** and **9** (See Scheme III).

5-Methyl-2-amino-1,3,4-thiadiazole (**10**) with dimethyl acetylenedicarboxylate gave only one isomer **11** which could be hydrolyzed and decarboxylated to compound **12**. This compound could also be synthesized directly from the reaction of 5-methyl-2-amino-1,3,4-thiadiazole and ehtyl propiolate. The ir, uv and nmr of compound **12** are significantly different from those reported for the structurally similar, but isomeric, 5-one **13** (8). We therefore assign the 7-one structure for **12**.

(Scheme III)



Hydrolysis, followed by decarboxylation of the selenadiazole product gave a compound with spectra similar to those of **12** and quite different from those of **13**. Therefore, the selenium compounds are assigned structure **8** (See Scheme III).

The mass spectra of the 5-one and the 7-one series were quite similar and could not be used to distinguish between the isomers as has been used previously for the isomeric oxadiazoles (6). The physical properties of the compounds prepared are summarized in Table II.

Next, the reaction of 5-substituted-2-amino-1,3,4-selenadiazoles with ethyl propiolate were studied. In this case however, the reaction took an unusual path. The major product from this reaction was a solid **15**; ir: ν 1678 (amide), 1738 (ester); uv λ max (ethanol): 363 (ε = 4.12), 342 (ε = 4.19), 258 (shoulder, ε = 3.34) 228 (ε = 4.20). The nmr consisted of a singlet, δ 8.77 (1H), a doublet 8.0 (1H, J = 7 Hz), a doublet 6.77 (1H, J = 7 Hz), a quartet 4.21 (2H) and a triplet 1.42 (3H). Its mass spectrum showed a molecular ion at 272 m/e with the characteristic

(Table II)

X	R	R'	MP, °C	Ir (cm^{-1})	Uv λ max (ethanol), (log ε)	Nmr (deuteriochloroform, δ)
Se	H	$COOCH_3$	167-168 (b)	1630	278 (3.97), 255 (4.20)	9.66 (s, 1H, H_2), 7.03 (s, 1H, H_6), 3.83 (s, 3H, OCH_3) (a)
Se	CH_3	$COOCH_3$	185-187 (b)	1640	278 (4.04), 255 (4.20)	6.36 (s, 1H, H_6), 4.08 (s, 3H, OCH_3), 2.80 (s, 3H, CH_3)
Se	CH_3	COOH	180-181 (c)	1625	272 (3.89), 218 (4.15)	
Se	CH_3	H	213-214 (d)	1635	274 (3.80), 220 (3.96)	8.17 (d, 1H, H_5, $J_{5,6}$ = 8 Hz), 6.4 (d, 1H, H_6, $J_{5,6}$ = 8 Hz), 2.73 (s, 3H, CH_3)
S	CH_3	$COOCH_3$	164-165 (b)	1640	267 (3.36), 213 (4.11)	6.63 (s, 1H, H_6), 4.03 (s, 3H, OCH_3), 2.73 (s, 3H, CH_3)
S	CH_3	COOH	148-150 (c)	1625	268 (3.96), 215 (4.34)	7.23 (s, 1H, H_6), 2.5 (s, 3H, CH_3) (a)
S	CH_3	H	207-208 (e)	1640	267 (3.36), 213 (4.11)	8.10 (d, 1H, H_5, $J_{5,6}$ = 7.5 Hz), 6.33 (d, 1H, H_6, $J_{5,6}$ = 7.5 Hz), 2.66 (s, 1H, CH_3) (a)
Se	C_2H_5	$COOCH_3$	104-106 (b)	1640	278 (3.76), 225 (3.86)	6.52 (s, 1H, H_6), 4.0 (s, 3H, OCH_3), 3.1 (q, 2H, CH_2), 1.23 (t, 3H, CH_3)
Se	C_2H_5	COOH	158-160 (c)	1635	277 (3.60), 222 (3.97)	7.0 (s, 1H, H_6), 2.70 (q, 2H, CH_2), 1.0 (t, 3H, CH_3) (a)
Se	C_2H_5	H	164-165 (f)	1645	275 (4.59), 220 (4.69)	8.26 (d, 1H, H_5, $J_{5,6}$ = 8 Hz), 6.33 (d, 1H, H_5, $J_{5,6}$ = 8 Hz), 3.05 (q, 2H, CH_2), 1.43 (t, 3H, CH_3)
Se	CF_3	$COOCH_3$	195-196 (b)	1670	293 (3.92), 226 (4.07)	6.77 (s, 1H, H_6), 4.03 (s, 3H, OCH_3)

(a) Nmr (trifluoroacetic acid). (b) Crystallized from ethanol. (c) Crystallized from water. (d) Crystallized from ethanol-ethyl acetate. (e) Crystallized from methanol. (f) Crystallized from ethyl acetate.

selenium isotopic abundance pattern. The above data can correspond to any of the four different structures A,B,C and D for compound **15**; although, ir and uv data favor structure C or D. In addition, when 5-ethyl-2-amino-1,3,4-selenadiazole was used a small amount of compound **14** (R = Et) was isolated. A possible route for the formation of this compound is shown in Scheme IV.

(Scheme IV)

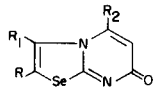
Indeed when compound **14** was reacted with ethyl propiolate compound **15** was formed in high yield. A possible mechanism for the formation of compound **15** is shown in Scheme V. As can be seen from this mechanism 2-substituted or 2,5-disubstituted-7*H*-1,3,4-selenadiazolo-

(Scheme V)

[3,2-*a*]pyrimidin-7-ones upon reaction with ethyl or methyl propiolate would lead to the conversion of selenadiazole moiety to selenazole ring system. In conformity with this mechanism acetonitrile was detected by gas chromato-

(Table III)

Chemical Shifts for Substituted-7*H*-selenazolo[3,2-*a*]pyrimidin-7-one in Trifluoroacetic Acid



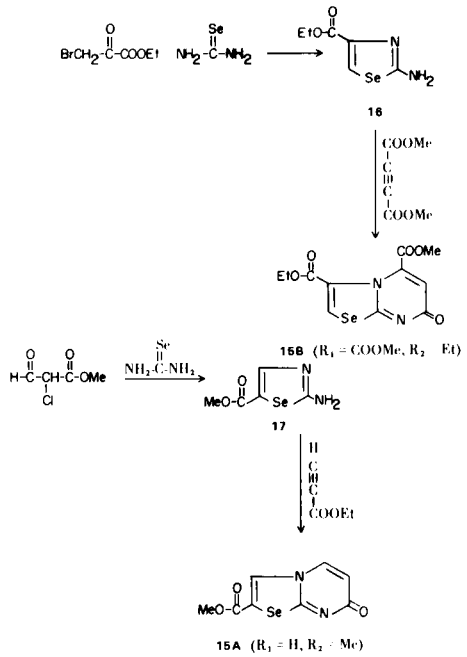
No.	R	R_1	R_2	H_2	H_3	H_5	H_6
4a	H	H	H	7.37	7.87	8.17	6.33
4b	H	CH_3	H	7.4	--	8.15	6.8
7a	H	H	$COOCH_3$	7.60	7.80	--	7.27
7c	H	C_6H_5	$COOCH_3$	7.50	--	--	6.70
15B	H	$COOC_2H_5$	$COOCH_3$	8.07	--	--	6.63 (a)
15A	$COOCH_3$	H	H	--	8.20	8.20	6.55

(a) In deuteriochloroform.

graphy when 2-methyl-7*H*-1,3,4-selenadiazolo[3,2-*a*]-pyrimidin-7-one (**14**, R = CH_3) was reacted with ethyl propiolate, also propionitrile was identified when 2-ethyl-5-carbomethoxy-7*H*-1,3,4-selenadiazolo[3,2-*a*]pyrimidin-7-one (**8**, R = C_2H_5) was reacted with ethyl propiolate.

Compounds **15A** and **15B** were synthesized from the corresponding aminoselenazoles (See Scheme VI), and were shown to be different from **15**. Therefore, **15** has structure C or D.

(Scheme VI)



The nmr spectra of all substituted-7*H*-1,3,4-selenadiazolo[3,2-*a*]pyrimidin-7-ones prepared are summarized in Table III. As it can be seen from this table, in all cases H_3 appears in lower field than H_2. The position of the proton 3 in compound **15A** appears at 8.2 ppm, showing the maximum down field shift in the series. The proton observing at 8.77 in the product under discussion is even lower than this figure. This could be in favor of **15C** rather than **15D** for the product; although, no clear cut proof for either of these two structures could be obtained.

EXPERIMENTAL

Melting points were determined on a Kofler hot stage microscope and are uncorrected. Nmr spectra were determined using Varian A-60A and T-60 spectrometers and chemical shifts (δ) are in ppm relative to tetramethylsilane. The ir spectra were obtained from a Leitz Model III spectrograph. Mass spectra were run on a Varian Model Mat CH5 instrument. Uv spectra were obtained using a Pye Unicam SP800 instrument. Glc analysis was carried out with a Perkin Elmer F-11 gas chromatograph using a 10% carbowax column (20 ft x 0.25 in.).

Reaction of 2-Aminoselenazole with Ethyl Propiolate.

A solution of 2-aminoselenazole (0.74 g., 0.005 mole) (9) and ethyl propiolate (0.49 g., 0.005 mole) in 20 ml. of tetrahydrofuran was allowed to stand at room temperature for 4 days. The precipitate was filtered and crystallized from DMSO to afford 0.5 g. (50%) of 7*H*-selenazolo[3,2-*a*]pyrimidin-7-one (**4a**), m.p. 276-278°; nmr (trifluoroacetic acid): 8.17 (d, 1H, H_5, $J_{5,6}$ = 7.8 Hz), 7.87 (d, 1H, H_3, $J_{2,3}$ = 5 Hz), 7.37 (d, 1H, H_2, $J_{2,3}$ = 5 Hz), and 6.33 (d, 1H, H_6, $J_{5,6}$ = 7.8 Hz).

Anal. Calcd. for $C_6H_4N_2OSe$: C, 36.18; H, 2.01; N, 14.07. Found: C, 36.12; H, 2.09; N, 13.96.

The tlc of the mother liquid (silica gel, chloroform:ethyl acetate, 7:3) afforded 300 mg. (23%) compound **5** (R = H), m.p. 84-85° (benzene-hexane); ir (potassium bromide): 1670 (ester), 1615 cm^{-1} (double bond); nmr (trifluoroacetic acid): 7.73 (d, 1H, H_6, $J_{6,7}$ = 14 Hz), 7.05 (s, 2H, selenazole-ring), 6.1 (d, 1H, H_7, $J_{6,7}$ = 14 Hz), 4.0 (q, 2H, OCH_2), and 0.97 (t, 3H, CH_3). The coupling constant confirms the *trans* configuration at the double bond; uv λ max (ethanol): 325 (ϵ = 3.91), 245 (ϵ = 4.10).

Anal. Calcd. for $C_8H_{10}N_2O_2Se$: C, 39.18; H, 4.08; N, 11.43. Found: C, 39.09; H, 4.22; N, 11.22.

In addition to compound **5** from tlc 50 mg. (2.9%) compound **6** (R = H), m.p. 153-154° (ethyl acetate:hexane) was isolated; ir (potassium bromide): 1695 (ester) 1620 cm^{-1} (double bond); nmr (deuteriochloroform): 8.40 (d, 1H, H_6, $J_{6,7}$ = 14 Hz), 7.47 (d, 1H, H_9, $J_{9,10}$ = 13 Hz), 7.07 (d, 1H, H_2 or $_3$, $J_{2,3}$ = 5 Hz), 6.80 (d, 1H, H_3 or $_2$, $J_{2,3}$ = 5 Hz), 6.07 (d, 1H, H_7, $J_{6,7}$ = 14 Hz), 5.87 (d, 1H, H_{10}, $J_{9,10}$ = 13 Hz), 4.20 (m, 4H, OCH_2) and 1.33 (unresolved t, 6H, CH_3). The coupling constants confirm the *trans* configurations at the double bonds; uv λ max (ethanol): 375 (ε = 4.44), 305 (ε = 4.13), 260 (ε = 4.25), 232 (ε = 4.44).

Anal. Calcd. for $C_{13}H_{16}N_2O_4Se$: C, 45.48; H, 4.66; N, 8.16. Found: C, 45.27; H, 4.67; N, 8.37.

Reaction of 4-Methyl-2-aminoselenazole with Ethyl Propiolate.

A solution of 4-methyl-2-aminoselenazole (1.62 g., 0.01 mole) and ethyl propiolate (0.98 g., 0.01 mole) in 40 ml. tetrahydrofuran was allowed to stand at room temperature for 4 days. The precipitate was filtered and crystallized from DMSO to give 1.1 g. (51%) of the compound **4b**, m.p. 298-300°; nmr (trifluoroacetic acid): 8.15 (d, 1H, H_5, $J_{5,6}$ = 7.5 Hz), 7.4 (s, 1H, H_2), 6.8 (d, 1H, H_6, $J_{5,6}$ = 7.5 Hz), and 2.2 (s, 3H, CH_3).

Anal. Calcd. for $C_7H_6N_2OSe$: C, 39.44; H, 2.82; N, 13.15. Found: C, 39.30; H, 2.68; N, 12.98.

The tlc of the mother liquid (silica gel, chloroform:ethyl acetate, 7:3) afforded 220 mg. of the compound **5** (R = CH_3), m.p. 106-108° (benzene-hexane); ir (potassium bromide): 1670 (ester), 1620 cm^{-1} (double bond); uv λ max (ethanol): 325 (ε = 4.11) 245 (ε = 4.16); nmr (trifluoroacetic acid): 7.13 (d, 1H, H_6, $J_{6,7}$ = 14 Hz), 6.53 (s, 1H, H_2), 6.13 (d, 1H, H_7, $J_{6,7}$ = 14 Hz), 4.0 (q, 2H, OCH_2), 1.77 (s, 3H, CH_3), and 0.90 (t, 3H, CH_3). The coupling constant confirms the *trans* configuration at the double bond.

Anal. Calcd. for $C_9H_{12}N_2O_2Se$: C, 41.70; H, 4.63; N, 10.81. Found: C, 41.58; H, 4.74; N, 10.81.

5-Carbomethoxy-7*H*-selenazolo[3,2-*a*]pyrimidin-7-one (**7a**).

A solution of 2-aminoselenazole (0.74 g., 0.005 mole) and dimethyl acetylendicarboxylate (0.71 g., 0.005 mole) in 50 ml. of tetrahydrofuran was allowed to stand at room temperature for 4 days. The precipitate was filtered and crystallized from DMSO-ethyl acetate to give 0.9 g. (70%) of compound **7a**, m.p. 157-158°; nmr (trifluoroacetic acid): 7.80 (d, 1H, H_3, $J_{2,3}$ = 5 Hz), 7.60 (d, 1H, H_2, $J_{2,3}$ = 5 Hz), 7.27 (s, 1H, H_6), and 3.70 (s, 3H, OCH_3).

Anal. Calcd. for $C_8H_6N_2O_3Se$: C, 37.35; H, 2.33; N, 10.89. Found: C, 37.08; H, 2.29; N, 10.89.

3-Phenyl-5-carbomethoxy-7*H*-selenazolo[3,2-*a*]pyrimidin-7-one (**7c**).

This compound was prepared similar to its hydrogen analogue form 4-phenyl-2-aminoselenazole and dimethyl acetylenedicarboxylate; nmr (trifluoroacetic acid): 7.50 (s, 1H, H_2), 7.0 (m, 5H, Ph), 3.70 (s, 1H, H_6), and 2.93 (s, 3H, OCH_3).

Anal. Calcd. for $C_{14}H_{10}N_2O_3Se$: C, 50.45; H, 3.00; N, 8.41. Found: C, 50.35; H, 2.88; N, 8.27.

Conversion of 5-Carbomethoxy-7*H*-selenazolo[3,2-*a*]pyrimidin-7-one (**7a**) to 7*H*-Selenazolo[3,2-*a*]pyrimidin-7-one (**4a**).

To a hot solution of 258 mg. (1 mmole) of compound **7a** in 10 ml. of methanol was gradually added a solution of 40 mg. (1 mmole) of sodium hydroxide in 1 ml. of water. After 5 minutes, methanol was evaporated and the solution acidified with dilute hydrochloric acid. The precipitate was crystallized from water to give 120 mg. of 5-carboxy-7*H*-selenazolo[3,2-*a*]pyrimidin-7-one, m.p. 195-196°. This compound was readily decarboxylated at 205° and gave **4a**, m.p. 276-278° (DMSO).

General Procedure for the Reaction of 5-Substituted-2-amino-1,3,4-selenadiazoles with Dimethyl Acetylenedicarboxylate.

A solution of 5-substituted-2-amino-1,3,4-selenadiazole (0.01 mole) (**2**) and dimethyl acetylenedicarboxylate (0.01 mole) in 20 ml. of methanol (or tetrahydrofuran) was refluxed for six hours. In most cases, after cooling the precipitate was filtered and crystallized from appropriate solvent (See Table II). If the product did not precipitate, the solvent was removed and the residue was chromatographed (tlc, silica gel) using chloroform:ethanol (95:5) as eluent. The major product was separated and crystallized. The yield was 40 to 60%.

2-Methyl-5-carbomethoxy-7*H*-1,3,4-selenadiazolo[3,2-*a*]pyrimidin-7-one (**8**, R = CH_3).

A solution of 5-methyl-2-amino-1,3,4-selenadiazole (1.62 g., 0.01 mole) (**2**) and dimethyl acetylenedicarboxylate (1.42 g., 0.01 mole) in 40 ml. of tetrahydrofuran was refluxed for six hours. The solvent was evaporated. To the residue 5 ml. of ethanol was added and the crystals were filtered. Recrystallization from ethanol gave 1.1 g. of the product (40%), m.p. 185-187°.

Anal. Calcd. for $C_8H_7N_3O_3Se$: C, 35.29; H, 2.57; N, 15.44. Found: C, 35.28; H, 2.57; N, 15.25.

Conversion of 2-Methyl-5-carbomethoxy-7*H*-1,3,4-selenadiazolo-[3,2-*a*]pyrimidin-7-one (**8**, R = CH_3) to 2-Methyl-7*H*-1,3,4-selenadiazolo[3,2-*a*]pyrimidin-7-one (**14**, R = CH_3).

To a hot solution of compound **8** (273 mg., 1 mmole) in 10 ml. of methanol was gradually added a solution of sodium hydroxide (40 mg., 1 mmole) in 20 ml. of water. After 10 minutes, methanol was evaporated. To the cold solution was added 0.1 ml. of acetic acid and 0.1 ml. of hydrochloric acid. The precipitate was crystallized from water to give 205 mg. (80%) of 2-methyl-5-carboxy-7*H*-1,3,4-selenadiazolo[3,2-*a*]pyrimidin-7-one. The acid (128 mg., 0.5 mmole) was heated at 190° for 10 minutes and the product was crystallized from ethanol-ethyl acetate to give 86 mg. (80%) of compound **14** (R = CH_3), m.p. 213-214°.

Anal. Calcd. for $C_6H_5N_3OSe$: C, 33.64; H, 2.34; N, 19.63. Found: C, 33.65; H, 2.38; N, 19.61.

2-Ethyl-7*H*-1,3,4-selenadiazolo[3,2-*a*]pyrimidin-7-one (**14**, R = C_2H_5).

This compound was prepared from compound **8** (R = C_2H_5) similar to its methyl analogue.

Anal. Calcd. for $C_7H_7N_3OSe$: C, 36.84; H, 3.07; N, 18.42. Found: C, 36.68; H, 3.06; N, 18.42.

2-Methyl-5-carbomethoxy-7*H*-1,3,4-thiadiazolo[3,2-*a*]pyrimidin-7-one (**11**).

A solution of 5-methyl-2-amino-1,3,4-thiadiazole (1.15 g., 0.01 mole) and dimethyl acetylenedicarboxylate (1.42 g., 0.01 mole) in 20 ml. of methanol was refluxed for 4 hours. The solution was concentrated and allowed to stand overnight. The precipitate was crystallized from ethanol to give the product (1.35 g., 60%), m.p. 164-165°.

Anal. Calcd. for $C_8H_7N_3O_3S$: C, 42.67; H, 3.11; N, 18.67. Found: C, 42.55; H, 3.02; N, 18.71.

2-Methyl-7*H*-1,3,4-thiadiazolo[3,2-*a*]pyrimidin-7-one (**12**).

To a hot solution of compound **11** (2.25 g., 0.01 mole) in 50 ml. of methanol was gradually added a solution of sodium hydroxide (0.4 g., 0.01 mole) in 10 ml. of water. After 10 minutes, methanol was evaporated and the solution was acidified with dilute hydro-

chloric acid. The precipitate was crystallized from water to give 2-methyl-5-carboxy-7*H*-1,3,4-thiadiazolo[3,2-*a*]pyrimidin-7-one (1.9 g., 90%), m.p. 148-150°. The acid (2.11 g., 0.01 mole) was heated at 160° for 5 minutes and then at 210° for additional 5 minutes. The residue was crystallized from methanol to give the compound **12** (1.5 g., 90%), m.p. 207-208°; m/e (%) 167 (M, 93), 139 (100), 126 (12), 100 (76), 98 (52), 85 (33), and 59 (76).

Anal. Calcd. for $C_6H_5N_3OS$: C, 43.11; H, 2.99; N, 25.15. Found: C, 43.25; H, 3.05; N, 25.21.

2,7-Dimethyl-5*H*-1,3,4-thiadiazolo[3,2-*a*]pyrimidin-5-one (**13**).

This compound was prepared from 5-methyl-2-amino-1,3,4 thiadiazole and ethyl acetoacetate according to Allen, *et al.*, (8) m.p. 144-145° (from ethanol); ir (potassium bromide): 1690 cm^{-1} (amide); uv λ max (ethanol): 305 (ε = 4.14), 235 (shoulder, ε = 3.90), and 214 (ε = 4.41); nmr (trifluoroacetic acid): 6.33 (s, 1H, H_6), 2.42 (s, 3H, CH_3), and 2.17 (s, 3H, CH_3); m/e (%) 181 (M, 82), 153 (61), 140 (5), 112 (100), 85 (75), and 59 (89).

Anal. Calcd. for $C_7H_7N_3OS$: C, 46.41; H, 3.87; N, 23.20. Found: C, 46.29; H, 3.90; N, 23.08.

Reaction of 5-Ethyl-2-amino-1,3,4-selenadiazole with Ethyl Propiolate.

A solution of 5-ethyl-2-amino-1,3,4-selenadiazole (1.77 g., 0.01 mole) and ethyl propiolate (1.96 g., 0.02 mole) in 25 ml. of ethanol was refluxed for 6 hours. The solution was concentrated (10 ml.). The precipitate was crystallized from ethanol to give 1.4 g. (52%) of 2 or 3-carbethoxy-5*H*-selenazolo[3,2-*a*]pyrimidin-5-one (15), m.p. 127-128°; ir (potassium bromide): 1678 (amide), 1738 cm^{-1} (ester); uv λ max (ethanol): 363 (ε = 4.12), 342 (ε = 4.19), 258 (shoulder, ε = 3.34), and 228 (ε = 4.20); nmr (deuteriochloroform): 8.77 (s, 1H, $H_{3 \text{ or } 2}$), 8.0 (d, 1H, H_7, $J_{6,7}$ = 7 Hz), 6.77 (d, 1H, H_6, $J_{6,7}$ = 7 Hz), 4.21 (q, 2H, OCH_2), and 1.42 (t, 3H, CH_3).

Anal. Calcd. for $C_9H_8N_2O_3Se$: C, 39.85; H, 2.95; N, 10.33. Found: C, 39.75; H, 2.85; N, 10.38.

Chromatography (tlc, silica gel, chloroform:methanol, 95:5) of the filtrate gave 30 mg. of the compound **14** (R = C_2H_5), m.p. 164-165° (ethyl acetate).

2 or 3-Carbomethoxy-5*H*-selenazolo[3,2-*a*]pyrimidin-5-one (**15C** or **15D**, R_1 = H, R_2 = CH_3).

This compound was prepared from 5-methyl-2-amino-1,3,4-selenadiazole and methyl propiolate in boiling methanol, m.p. 195-196° (methanol); ir (potassium bromide): 1678 (amide), 1735 cm^{-1} (ester); uv λ max (ethanol): 363 (ε = 4.07), 345 (ε = 4.16), 255 (shoulder, ε = 3.45) and 229 (ε = 4.20); nmr (deuteriochloroform): 8.72 (s, 1H, $H_{3 \text{ or } 2}$), 8.0 (d, 1H, H_7, $J_{6,7}$ = 7 Hz), 6.40 (d, 1H, H_6, $J_{6,7}$ = 7 Hz), and 4.0 (S, 3H, OCH_3): m/e 258 (M), 230, 199, 174, 164, 149, and 105.

Anal. Calcd. for $C_8H_6N_2O_3Se$: C, 37.35; H, 2.33; N, 10.89. Found: C, 37.35; H, 2.37; N, 10.79.

Reaction of 2-Methyl-7*H*-1,3,4-selenadiazolo[3,2-*a*]pyrimidin-7-one (**14**, R = CH_3) with Ethyl Propiolate.

A solution of **14** (R = CH_3, 2.15 g., 0.01 mole) and ethyl propiolate (0.98 g., 0.01 mole) in 15 ml. of ethanol was refluxed for 5 hours. After cooling, the crystals were filtered to give 2 or 3-carbethoxy-5*H*-selenazolo[3,2-*a*]pyrimidin-5-one (**15C** or **15D**, R_1 = H, R_2 = ethyl, 2.45 g., 90%), m.p. 127-128°.

The mother liquid was subjected to glc. The acetonitrile was detected by comparison with an authentic sample of pure acetonitrile.

Reaction of 2-Ethyl-5-carbomethoxy-7*H*-1,3,4-selenadiazolo[3,2-*a*]-pyrimidin-7-one (**8**, R = C_2H_5) with Ethyl Propiolate.

A solution of **8** (R = C_2H_5, 286 mg., 1 mmole) and ethyl propiolate (98 mg., 1 mmole) in 5 ml. of ethanol was refluxed for 3 hours. After cooling, the crystals were collected to give 2 or 3-carbethoxy-7-carbomethoxy-5*H*-selenazolo[3,2-*a*]pyrimidin-5-one (**15C** or **15D**, R_1 = $COOCH_3$, R_2 = C_2H_5, 270 mg., 82%), m.p. 140-142°; ir (potassium bromide): 1700 (amide), 1718 (ester), 1738 cm^{-1} (ester); uv λ max (ethanol): 374 (ε = 4.20), 366 (ε = 4.26), 265 (shoulder, ε = 4.04), and 236 (ε = 4.48); nmr (deuteriochloroform): 8.70 (s, 1H, $H_{2 \text{ or } 3}$), 7.10 (s, 1H, H_6), 4.43 (q, 2H, OCH_2), 4.0 (s, 3H, OCH_3), and 1.40 (t, 3H, CH_3); m/e 330 (M).

Anal. Calcd. for $C_{11}H_{10}N_2O_5Se$: C, 40.12; H, 3.04; N, 8.51. Found: C, 39.92; H, 3.14; N, 8.54.

In the mother liquid propionitrile was detected (glc) by comparison with an authentic sample of pure propionitrile.

4-Carbethoxy-2-aminoselenazole (**16**).

A mixture of ethyl bromopyruvate (1.95 g., 0.01 mole) and selenourea (1.23 g., 0.01 mole) was melted. After cooling, the mixture was neutralized (ammonia), and extracted with ethyl acetate. After evaporation of the solvent, the residue was crystallized from ethanol to give 1.8 g. (82%) of the product, m.p. 203-204°; ir (potassium bromide): 3450 and 3260 (amine, 1695 cm^{-1} (ester); nmr (trifluoroacetic acid): 7.87 (s, 1H, H_5), 4.02 (q, 2H, OCH_2), and 1.0 (t, 3H, CH_3).

Anal. Calcd. for $C_6H_8N_2O_2Se$: C, 32.88; H, 3.65; N, 12.79. Found: C, 32.90; H, 3.59; N, 12.68.

3-Carbethoxy-5-carbomethoxy-7*H*-selenazolo[3,2-*a*]pyrimidin-7-one (**15B**, R_1 = $COOCH_3$, R_2 = C_2H_5).

A solution of 4-carbethoxy-2-aminoselenazole (220 mg., 1 mmole) and dimethyl acetylenedicarboxylate (142 mg., 1 mmole) in 40 ml. tetrahydrofuran was refluxed for 36 hours. The solvent was evaporated. The chromatography of the residue afforded 65 mg. of the product (20%), m.p. 127-129° (benzene-hexane); ir (chloroform): 1640 (amide), 1720 cm^{-1} (ester); uv λ max (ethanol): 290, 242, and 210; nmr (deuteriochloroform): 8.07 (s, 1H, H_2), 6.63 (s, 1H, H_6), 4.23 (q, 2H, OCH_2), 3.83 (s, 3H, OCH_3), and 1.26 (t, 3H, CH_3).

Anal. Calcd. for $C_{11}H_{10}N_2O_5Se$: C, 40.12; H, 3.04; N, 8.51. Found: C, 40.18; H, 3.21; N, 8.38.

5-Carbomethoxy-2-aminoselenazole (**17**).

A mixture of methyl formylchloroacetate (1.36 g., 0.01 mole) (**11**) and selenourea (1.23 g., 0.01 mole) in 10 ml. water was heated at 50° for 1 hour. The solution was neutralized and extracted with ethyl acetate. Evaporation of the solvent and crystallization from methanol gave 1.7 g. product (82%), m.p. 202-203°.

Anal. Calcd. for $C_5H_6N_2O_2Se$: C, 29.27; H, 2.93; N, 13.66. Found: C, 29.28; H, 3.02; N, 13.45.

2-Carbomethoxy-7*H*-selenazolo[3,2-*a*]pyrimidin-7-one (**15A**, R_1 = H, R_2 = CH_3).

A solution of **17** (2.06 g., 0.01 mole) and ethyl propiolate (0.98 g., 0.01 mole in 20 ml. of methanol was refluxed for 4 hours. After cooling the precipitate was filtered and crystallized from DMSO to give 1.58 g., product (58%); m.p. 245-246°; ir (potassium bromide): 1640 (amide), 1720 cm^{-1} (ester); uv λ max (ethanol): 307 (ε = 4.31), and 230 (ε = 4.23); nmr (trifluoroacetic acid): 8.20 (s, 1H, H_3), 8.20 (d, 1H, H_5, $J_{5,6}$ = 8 Hz), 6.55 (d, 1H, H_6, $J_{5,6}$ = 8 Hz), and 3.57 (s, 3H, OCH_3); m/e 258 (M), 230, 199,

164, 149, and 105.

Anal. Calcd. for $C_8H_6N_2O_3Se$: C, 37.35; H, 2.33; N, 10.89. Found: C, 37.32; H, 2.29; N, 10.78.

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