

Victor Israel Cohen

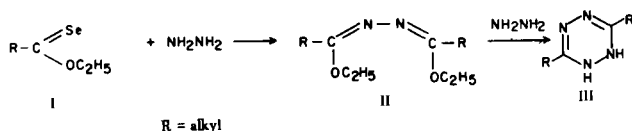
Organic Chemistry Laboratory, Sciences Faculty, Ferdowsi University, Mashhad, Iran
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Some 3,6-dialkyl, diaryl and diheterocyclic-1,2-dihydro-1,2,4,5-tetrazines have been synthesized from the action of hydrazine on aliphatic selenonesters, and aromatic and heterocyclic selenoamides.

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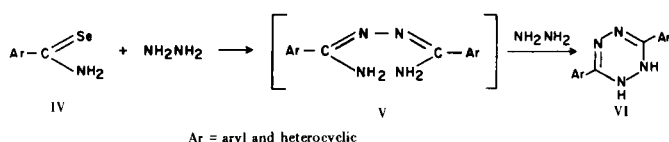
Our interest in tetrazine compounds prompted us to try two new possible methods for their synthesis. In the first method (Scheme 1), 2 moles of selenonesters I reacted with 1 mole of hydrazine hydrate in methanol to yield compounds II, which by reaction with another mole of hydrazine gave 3,6-dialkyl-1,2-dihydro-1,2,4,5-tetrazines (III).

Scheme 1

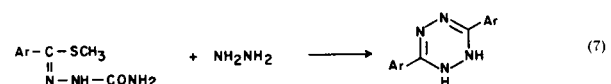
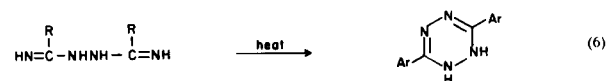
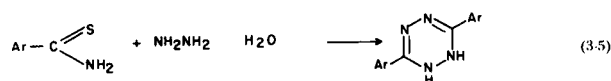
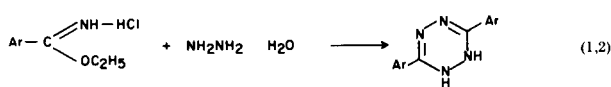


In the second method (Scheme 2), aromatic or heterocyclic selenoamides (IV) reacted with hydrazine in an analogous manner to selenonesters, to yield in the first step compounds V. The reaction of V with another mole of hydrazine gave 3,6-diaryl-1,2,4,5-tetrazines (VI).

Scheme 2



The availability of the starting materials and the simplicity of these procedures provide an easy route to 3,6-disubstituted-1,2-dihydro-1,2,4,5-tetrazines, which have earlier been prepared by the following methods:



The nmr and mass spectral data of the above mentioned compounds are listed in Table I.

EXPERIMENTAL

The melting points were determined by a Kofler Hot-Bench and Maquenne Block apparatus. The pmr spectra were recorded on a Varian EM-360 spectrometer using TMS as internal standard; the chemical shift values are expressed in ppm (δ). The mass spectra were determined by a Varian Mat apparatus at 96 eV and at 25-140° by direct insertion into the ion source. All the analyses were performed by Dornis u. Kolbe, Hohenweg 17, West Germany. Selenonesters were obtained according to the literature (8). The method of preparation of aromatic and heterocyclic selenoamides is given in reference 9.

3,6-Dialkyl-1,2-dihydro-1,2,4,5-tetrazines, General Procedure.

To a solution of 1.51 g. (0.01 mole) of *O*-ethyl selenoacetate in 10 ml. of methanol was added an excess of hydrazine hydrate in methanol. After 7 days at room temperature, the elemental selenium was removed by filtration. Elimination of the solvent in a rotary film evaporator left a solid which on crystallization in pyridine gave 0.73 g. (65%) of 1 (Table II).

3,6-Diaryl and Diheterocyclic-1,2-dihydro-1,2,4,5-tetrazines, General Procedure.

To a solution of 1.98 g. (0.01 mole) of *m*-tolylselenoamide in methanol at 0° was added dropwise an excess solution of hydrazine hydrate in methanol. After 7 days in refrigeration, the solid was collected. Recrystallization from ethanol provided 7 (Table II) (35%), m.p. 203°.

3,6-Diaryl and Diheterocyclic-1,2,4,5-tetrazines, General Procedure.

Following the general procedure described above with slight modification, we have obtained in some cases 3,6-disubstituted tetrazines.

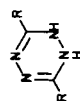
To a hot solution of 1.84 g. (0.01 mole) of benzselenoamide in methanol was added an excess solution of hydrazine hydrate in methanol. After 7 days at room temperature, the solid was collected. Recrystallization from ethanol provided 14 (Table III) (55%) m.p. 188°.

The nmr and mass spectral data for the 3,6-diaryl and diheterocyclic tetrazines prepared are listed in Table IV.

REFERENCES AND NOTES

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- (2) P. Yates and O. Meresz, *Tetrahedron Letters*, 77 (1967).
- (3) K. Nakahara and M. Ohta, *Nippon Kagaku Zasshi*, **77**, 388 (1956).
- (4) A. Spasov and E. Golovinsku, *C. R. Acad. Bulg. Sci.*, **14**,

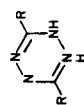
Table I
Mass and Nmr Spectral Data of 3,6-Di-substituted 1,2-Dihydro-1,2,4,5-tetrazines



Compound No.	R	Ms m/e (%)	Molecular Formula	Chemical Shifts, ppm δ (a)
1	CH ₃	30 (18); 42 (100); 112 (38)	C ₄ H ₈ N ₄ (112)	2.22 (6H, s); 5.73 (2H, s)
2	CH ₃ CH ₂	27 (22); 29 (34); 30 (13); 39 (12); 41 (9); 43 (10); 54 (11); 56 (100); 57 (43); 124 (40); 139 (55); 140 (87)	C ₆ H ₁₂ N ₄ (140)	1.20 (6H, t); 2.68 (4H, q); 5.75 (2H, s)
3	CH ₃ (CH ₂) ₂	27 (19); 29 (7); 39 (8); 41 (20); 43 (26); 57 (9); 70 (12); 112 (29); 125 (13); 140 (100); 153 (10); 167 (5); 168 (8)	C ₈ H ₁₆ N ₄ (168)	0.90 (6H, t); 1.63 (4H, m); 2.60 (4H, t); 5.72 (2H, s)
4	$\begin{matrix} \text{CH}_3 \\ \\ \text{CH}_3\text{CH} \end{matrix}$	27 (28); 39 (12); 41 (29); 43 (100); 54 (13); 70 (50); 140 (10); 153 (20); 168 (90)	C ₈ H ₁₆ N ₄ (168)	1.02 (12H, d); 2.20 (2H, q); 7.80 (2H, s)
5	CH ₃ (CH ₂) ₃	27 (15); 29 (20); 39 (10); 41 (25); 43 (33); 112 (25); 126 (10); 139 (11); 154 (100); 167 (19); 181 (5); 195 (2); 196 (1)	C ₁₀ H ₂₀ N ₄ (198)	0.90 (6H, t); 1.50 (8H, brm); 2.63 (4H, t); 5.72 (2H, s)
6	CH ₃ (CH ₂) ₄	27 (15); 29 (21); 39 (10); 41 (26); 43 (27); 51 (10); 112 (19); 126 (20); 139 (14); 153 (7); 168 (100); 181 (38); 195 (12); 223 (2); 224 (5)	C ₁₂ H ₂₄ N ₄ (224)	0.09 (6H, t); 1.50 (12H, brm); 2.63 (4H, t); 5.72 (2H, s)
7	3-CH ₃ -C ₆ H ₄	39 (5); 65 (15); 91 (29); 118 (90); 264 (100)	C ₁₆ H ₁₆ N ₄ (264)	2.35 (6H, s); 7.30 (2H, m); 7.66 (6H, m); 9.00 (2H, s)
8	4-CH ₃ -C ₆ H ₄	39 (8); 65 (18); 89 (7); 90 (8); 91 (29); 116 (8); 117 (14); 118 (100); 132 (3); 146 (3); 264 (90)	C ₁₆ H ₁₆ N ₄ (264)	2.38 (6H, s); 7.30 (4H, m); 7.80 (4H, m); 8.95 (2H, s)
9	4-CH ₃ O-C ₆ H ₄	39 (7); 64 (8); 77 (8); 90 (12); 91 (17); 103 (7); 119 (14); 133 (25); 134 (100); 296 (96)	C ₁₆ H ₁₆ N ₄ O ₂ (296)	3.82 (6H, s); 7.01 (4H, m); 7.78 (4H, m); 8.88 (2H, s)
10	4-BrC ₆ H ₄	50 (15); 51 (20); 102 (97); 181 (100); 183 (98); 390 (5); 392 (11); 394 (8)	C ₁₄ H ₁₀ N ₄ Br ₂ (390-392-394)	
11	4-ClC ₆ H ₄	50 (14); 51 (13); 75 (23); 102 (36); 111 (15); 137 (100); 138 (65); 139 (39); 140 (22); 304 (50); 306 (31)	C ₁₄ H ₁₀ N ₄ Cl ₂ (304-306)	
12	3,5-(CH ₃ O) ₂ C ₆ H ₃	65 (11); 77 (13); 90 (8); 103 (17); 106 (8); 120 (6); 121 (9); 122 (10); 133 (14); 134 (11); 163 (63); 164 (78); 354 (10); 356 (100); 357 (15)	C ₁₈ H ₂₀ N ₄ O ₄ (356)	3.80 (12, s); 6.60 (4H, m); 7.00 (2H, d); 9.02 (2H, s)
13	2-Pyridyl	51 (26); 78 (54); 79 (19); 105 (100); 238 (71)	C ₁₂ H ₁₀ N ₆ (238)	7.25 (2H, m); 7.60 (2H, m); 7.90 (2H, m); 8.60 (2H, m); 9.00 (2H, s)

(a) Recorded in DMSO-d₆.

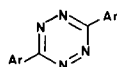
Table II
Physical Properties and Microanalytical Data of 3,6-Disubstituted 1,2-Dihydro-1,2,4,5-tetrazines



Compound No.	R	Time of Contact and Temperature	M.p. °C	Crystallization Solvent	Yield %	Empirical Formula	Elemental Analysis (%)		
							C	H	N
1	CH ₃	7 days/room temp.	199	pyridine	65	C ₄ H ₈ N ₄	Calcd. 42.88 Found 42.86	7.14 7.18	49.98 50.05
2	CH ₃ CH ₂	7 days/room temp.	164	chloroform-petroleum ether	80	C ₆ H ₁₂ N ₄	Calcd. 51.45 Found 51.30	8.57 8.50	39.98 40.18
3	CH ₃ (CH ₂) ₂	7 days/room temp.	172	chloroform-petroleum ether	85	C ₈ H ₁₆ N ₄	Calcd. 57.16 Found 57.12	9.52 9.53	33.32 33.38
4	$\begin{matrix} \text{CH}_3 \\ \\ \text{CH}_3\text{CH} \end{matrix}$	7 days/room temp.	167	hexane	90	C ₈ H ₁₆ N ₄	Calcd. 57.16 Found 57.16	9.52 9.55	33.32 33.33
5	CH ₃ (CH ₂) ₃	7 days/room temp.	163	ethanol-water	92	C ₁₀ H ₂₀ N ₄	Calcd. 61.24 Found 61.06	10.20 10.15	28.56 28.75
6	CH ₃ (CH ₂) ₄	7 days/room temp.	154	ethanol-water	92	C ₁₂ H ₂₄ N ₄	Calcd. 64.30 Found 64.25	10.73 10.73	25.08 25.08
7	3-CH ₃ -C ₆ H ₄	7 days/refrigeration	203	<i>n</i> -propanol	35	C ₁₆ H ₁₆ N ₄	Calcd. 72.74 Found 72.75	6.06 5.98	21.20 21.30
8	4-CH ₃ -C ₆ H ₄	7 days/room temp.	156	<i>n</i> -butanol	93	C ₁₆ H ₁₆ N ₄	Calcd. 72.74 Found 72.80	6.06 6.05	21.20 21.17
9	4-CH ₃ O-C ₆ H ₄	7 days/room temp.	255	anisole	85	C ₁₆ H ₁₆ N ₄ O ₂	Calcd. 64.89 Found 64.83	5.40 5.38	18.91 18.96
10	4-Br-C ₆ H ₄	7 days/room temp.	310	<i>n</i> -butylacetate	50	C ₁₄ H ₁₀ Br ₂ N ₄	Calcd. 42.68 Found 42.70	2.54 2.56	14.22 14.27
11	4-ClC ₆ H ₄	7 days/refrigeration	252	<i>n</i> -butanol	46	C ₁₄ H ₁₀ Cl ₂ N ₄	Calcd. 55.12 Found 55.09	3.28 3.33	18.36 18.09
12	3,5-(CH ₃ O) ₂ C ₆ H ₃	7 days/room temp.	188	<i>n</i> -butanol	80	C ₁₈ H ₂₀ N ₄ O ₄	Calcd. 60.70 Found 60.69	5.62 5.57	15.72 15.70
13	2-pyridyl	7 days/refrigeration	199	<i>n</i> -propanol	65	C ₁₂ H ₁₀ N ₆	Calcd. 60.52 Found 60.46	4.20 4.23	35.28 35.44

Table III

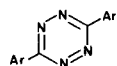
Physical Properties and Microanalytical Data of 3,6-Disubstituted 1,2,4,5-Tetrazines



Compound No.	Ar	M.p. °C	Crystallization Solvent	Yield %	Empirical Formula	Elemental Analysis (%)				
						C	H	N	S	
14	C ₆ H ₅	188	ethanol	55	C ₁₄ H ₁₀ N ₄	Calcd.	71.81	4.27	23.92	
						Found	71.87	4.31	23.90	
15	3-CH ₃ C ₆ H ₄	151	ethanol	58	C ₁₆ H ₁₄ N ₄	Calcd.	73.30	5.34	21.36	
						Found	72.85	5.55	21.33	
16	2-Thienyl	186	ethanol	90	C ₁₀ H ₆ N ₄ S ₂	Calcd.	48.78	2.44	22.74	26.04
						Found	48.73	2.43	22.70	26.16

Table IV

Mass and Nmr Spectral Data of Some 3,6-Disubstituted-1,2,4,5-tetrazines



Compound No.	Ar	Ms m/e (%)	Molecular Formula	Chemical Shifts, ppm δ (a)
14	C ₆ H ₅	39 (7); 43 (16); 50 (9); 51 (6); 76 (21); 77 (8); 103 (100); 234 (5)	C ₁₄ H ₁₀ N ₄ (234)	7.48 (4H, m); 7.82 (4H, m)
15	3-CH ₃ C ₆ H ₄	19 (7); 89 (12); 90 (20); 117 (100); 262 (11)	C ₁₆ H ₁₄ N ₄ (262)	2.48 (6H, s); 7.51 (4H, m); 8.32 (4H, m)
16	2-Thienyl	39 (9); 45 (29); 58 (19); 64 (7); 70 (6); 82 (3); 109 (100); 246 (11)	C ₁₀ H ₆ N ₄ S ₂ (246)	7.32 (2H, m); 7.80 (2H, m); 8.15 (2H, m)

(a) Recorded in DMSO-*d*₆

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