Mar. 1978 Preparation of some 3-Hydroxy- and 3-Mercapto-1,2,4-triazoles. Reaction of Aliphatic Selenone Esters with Semicarbazide and

Thiosemicarbazide Derivatives

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The synthesis, mass and nmr spectra of a number of 3-hydroxy- and 3-mercapto-1,2,4-triazoles has been described.

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The synthesis of 3-hydroxy-1,2,4-triazoles from thioanilides and ethyl hydrazinocarbonate has been reported (1).

Similar products were also obtained by Pesson and Dupin (2) from esters and 4-phenylsemicarbazide.

Greenfield, et al., (3) and Pesson and co-workers (4), obtained mercaptotriazoles from 4-substituted thiosemicarbazide and esters using a methanolic sodium methoxide solution.

Treatment of 4-substituted thiosemicarbazide with RCOCl also provides 3-mercapto-1,2,4-triazoles (5).

These methods of synthesizing 3-hydroxy- and 3-mercapto-1,2,4-triazoles are either not general, or require restrictive conditions. We find that a simplified one step procedure giving the above mentioned products in good yields can be carried out in the following way: 3-mercapto- and 3-hydroxy-1,2,4-triazoles (4) can be prepared in good yields from the reaction of selenone esters (2) with thiosemicarbazide and 4-substituted semi- and thio-

Table I

Chemical Shifts Data of 3-Hydroxy- and 3-Mercapto-1,2,4-triazoles Derivatives

				R XH
Compound No.	R	R'	X	Nmr (a)
1 2 3 4 5 6	CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ (CH ₂) ₂ CH ₃ (CH ₂) ₃	H H C ₆ H ₅ C ₆ H ₅ C ₆ H ₅	S S S S S	2.20 δ (3H, s), 6.93 (1H, br s) 1.15 δ (3H, t), 2.55 (2H, q), 3.38 (1H, br s) 2.10 δ (3H, s), 7.55 (5H, s) 1.04 δ (3H, t), 2.40 (2H, q), 7.52 (5H, s) 0.85 δ (3H, t), 1.46 (2H, m), 2.36 (2H, t), 7.50 (5H, m) 0.83 δ (3H, t), 1.38 (4H, m), 2.45 (2H, t), 7.52 (5H, m) 2.28 δ (3H, s), 3.38 (3H, s)
7	CH ₃	CH ₃	S	2.28 8 (3H, 8), 3.30 (3H, 8)
8 9	CH ₃ CH ₃ -CH(CH ₂) ₂ CH ₃ CH ₂	CH₃ CH₃CH₂	s s	0.92 δ (6H, d), 1.55 (3H, m), 2.93 (2H, t), 3.42 (3H, s) 1.20 δ (3H, t), 1.22 (3H, t), 2.73 (2H, q), 3.93 (2H, q)
10 11 12 13	CH ₃ CH CH ₃ CH CH ₃ (CH ₂) ₃ CH ₃ CH ₃ CH ₂	$\begin{array}{c} \mathrm{CH_3CH_2} \\ \mathrm{CH_3CH_2} \\ \mathrm{C_6H_5} \\ \mathrm{C_6H_5} \end{array}$	S S O O	1.22 δ (6H, d), 1.25 (3H, t), 3.20 (1H, m), 3.98 (2H, q) 1.00 δ (3H, t), 1.25 (3H, t), 1.55 (4H, m), 2.77 (2H, t), 3.95 (2H, q) 1.90 δ (3H, s), 7.30 (5H, br m) 1.23 δ (3H, t), 2.50 (2H, q), 7.35 (5H, br m)
14 15	CH ₃ CH ₃ CH CH ₃ (CH ₂) ₃	C_6H_5 C_6H_5	0	1.00 δ (6H, d), 2.67 (1H, q), 7.48 (5H, s) 0.78 δ (3H, t), 1.30 (4H, br s), 2.45 (2H, t), 7.45 (5H, s)

(a) In DMSO-d₆ with TMS as the internal reference.

Table II

Derivatives

Mass Spectral Data of 3-Hydroxy- and 3-Mercapto-1,2,5-triazoles

Molecular Compound Formula No. m/e 1 32 (11), 42 (17), 57 (13), 59 (30), $C_3H_5N_3S$ 60 (21), 74 (100), 115 (66) (115)2 27(15), 29(10), 39(14), 41(29), $C_4H_7N_3S$ 42 (9), 43 (8), 45 (7), 55 (14), (129)56 (18), 59 (6), 60 (7), 70 (45), 74 (10), 114 (6), 128 (44), 129 (100), 130(7)3 27(11), 39(10), 51(31), 56(36), C9H9N3S 77 (45), 91 (11), 118 (12), 149 (191)(24), 190 (80), 191 (100) 4 39 (9), 41 (9), 51 (15), 70 (14), $C_{10}H_{11}N_{3}S$ 77 (25), 91 (21), 149 (14), 204 (205)(80), 205 (100) 5 39 (10), 41 (10), 51 (17), 55 (11), $C_{11}H_{13}N_{3}S$ 77 (30), 105 (24), 118 (12), 149 (219)(12), 150(12), 189(13), 190(38), 204 (36), 218 (37), 219 (100), 220 (16) 6 41 (12), 51 (13), 77 (27), 91 (13), $C_{12}H_{15}N_3S$ 118 (17), 149 (11), 190 (21), 191 (233)(53), 204(39), 232(24), 233(100) 7 32 (8), 41 (9), 42 (23), 43 (24), C4H7N3S 55(25), 56(41), 60(21), 129(100) (129)8 32 (19), 39 (10), 41 (15), 42 (16), $C_8H_{15}N_3S$ 55 (21), 56 (29), 60 (10), 74 (17), (185)105 (18), 129 (100), 142 (21), 170 (28), 185 (54) 9 29 (17), 41 (13), 56 (15), 60 (12), $C_6H_{11}N_3S$ 69 (20), 70 (24), 128 (32), 129 (157)(31), 156 (40), 157 (100) 10 27 (48), 29 (55), 41 (32), 42 (27), $C_7H_{13}N_3S$ 48 (59), 44 (68), 55 (24), 60 (70), (171)69 (28), 74(22), 84 (27), 88 (29), 102 (50), 119 (14), 128 (24), 143 (41), 156 (100), 159 (24), 170 (22), 171 (94) 11 27(29), 29(32.5), 30(20), 32(7), $C_8H_{15}N_3S$ 39 (10), 41 (20.5), 42 (10), 43 (185)(20), 44 (20.5), 55 (11.5), 59 (13), 60 (20.5), 69 (8.5), 71 (10), 74 (10), 88 (8), 102 (6.5), 115 (9), 128 (4.5), 142 (8), 143 (100), 144 (8), 156(15.5), 170(7.5), 185(15) 12 32 (29), 39 (21), 42 (23), 56 (20), C9H9N3O 65 (25), 66 (26), 77 (22), 92 (21), (175)93 (100), 114 (93), 119 (30), 175 13 39 (20), 41 (30), 51 (32), 70 (79), $C_{10}H_{11}N_3O$ 77 (40), 91 (73), 104 (13), 118 (189)(11), 132(11), 188(36), 189(100),

190 (14)

Table II (Continued)

Compound No.	MS; m/e (%)	Molecular Formula m/e
14	39 (23), 41 (20), 43 (25), 51 (27), 55 (19), 65 (12), 69 (11), 77 (33), 84 (32), 91 (39), 99 (7), 104 (12), 105 (37), 112 (14), 118 (13), 146 (3), 173 (6), 175 (5), 188 (43), 202 (29), 203 (100), 204 (13)	C ₁₁ H ₁₃ N ₃ O (203)
15	39 (8), 41 (11), 51 (11), 77 (18), 91 (12), 174 (33), 175 (100), 188 (10), 217 (34)	$C_{12}H_{15}N_3O$ (217)

semicarbazides (1). The reaction takes place through a stage involving the formation of the hydrazones 3, which eliminate a molecule of hydrogen selenide under the reaction conditions and are converted into the derivatives 4. In fact, we were able to isolate such a hydrazone 3 during brief heating of compound 1 with 2.

RNHCNHNH2 + R'C
$$OC_2H_5$$
 OC_2H_5 OC_2H_5

The nmr and mass spectral fragmentation of the aforementioned compounds are listed in Tables I and II.

EXPERIMENTAL

The nmr spectra were obtained on a Varian EM-360 spectrometer. Mass spectra were taken on a Varian CH7A Mass spectrometer. The elemental analyses were performed by Dornis und Kolbe Mikroanalytisches Laboratorium, Hohenweg 17, West Germany and Service Central de Microanalyses (C.N.R.S.) 2, Rue Henry Dunant-94320 Thiais, France. Melting points were measured on a Kofler hot bench apparatus. All of the semicarbazide and thiosemicarbazide derivatives were purchased from commercial sources. Aliphatic selenone esters were prepared from the corresponding iminoester (6).

Propyl Selenoester-4-phenylsemicarbazone.

4-Phenylsemicarbazide (1.51 g., 0.01 mole) was dissolved in anhydrous methanol and propyl selenonester (1.79 g., 0.01 mole) in 10 ml. of methanol was added. The mixture was heated under reflux for 1 hour and allowed to stand at room temperature for 1 day then the suspension which resulted was filtered. Evaporation of the solvent leaves 2 g. of semicarbazone (80%); m.p. (after two recrystallizations from anhydrous ethanol) 120°; ir (tablet with potassium bromide): 1675 cm⁻¹ (C=N); ms: 249 (85), 204 (8), 130 (42), 102 (50), 93 (100), 77 (30), 74 (28), 71 (50), 70 (32), 43 (63); ¹H nmr: 0.90 & (3H, t), 1.25 (3H, t), 1.62 (2H, m), 2.40 (2H, t), 4.16 (2H, q), 7.32 (5H, m), 8.30 (1H, s?), 9.11 (1H, s?) (1n DMSO-d₆ with TMS as the internal reference).

Anal. Calcd. for $C_{13}H_{19}N_3O_2$: C, 62.25; H, 7.63; N, 16.86. Found: C, 62.50; H, 7.66; N, 16.95.

 $Table\ III$ Physical Properties of 3-Hydroxy- and 3-Mercapto-1,2,4-triazoles Derivatives

Compound No.	R	R'	X	Reaction Solvent	Time of Reflux	B.p. °C (mm) (M.p. °C)	Crystallization Solvent	Yield %
1	CH ₃	Н	S	1-Butanol	48	(216)	Ethanol- Petroleum ether	70
2	CH₃CH₂	Н	S	1-Butanol	35 .	(174)	1-Butanol- Petroleum ether	74
3	CH ₃	C_6H_5	S	Methanol	50	(222)	n-Butyl acetate	87
4	CH ₃ CH ₂	C_6H_5	S	Methanol	50	(171)	n-Butyl acetate	75
5	$CH_3(CH_2)_2$	C_6H_5	S	Methanol	50	(148)	n-Butyl acetate	65
6	$CH_3(CH_2)_3$	C_6H_5	S	Methanol	50	(121)	Benzene	82
7	CH ₃	CH ₃	S	Methanol	50	(209)	n-Butyl acetate	68
8	CH ₃ CH ₃ -CH(CH ₂) ₂	CH ₃	S	Methanol	50	(104)	n-Butyl acetate- Petroleum ether	52
9	CH ₃ CH ₂	CH₃CH₂	S	Methanol	50	(144)	n-Butyl acetate- Petroleum ether	45
	CH ₃							
10	сн₃сн	CH ₃ CH ₂	S	Methanol	50	148(1)		62
11	CH ₃ (CH ₂) ₃	CH_3CH_2	\mathbf{s}	Methanol	3	204(1)		72
12	CH ₃	C_6H_5	O	Methanol	25	(233)	Pyridine- Ethyl ether	80
13	CH ₃ CH ₂	C_6H_5	0	Methanol	50	(127)	n-Butyl acetate- Petroleum ether	71
14	CH₃ CH₃-ĊH	C_6H_5	o	Methanol	50	(156)	n-Butyl acetate- Petroleum ether	68
15	CH ₃ (CH ₂) ₃	C_6H_5	0	Methanol	50	(124)	n-Butyl acetate- Petroleum ether	78

Table IV

Microanalytical Data of the Compounds Listed In Table III

C1	Empirical Formula	Elemental Analysis (%)					
Compound No.			С	Н	N	S	
1	$C_3H_5N_3S$	Caled. Found	$\frac{31.30}{31.43}$	4.34 4.54	36.52 36.19	27.82 27.57	
2	$C_4H_7N_3S$	Calcd. Found	$37.22 \\ 37.14$	5.42 5.38	$32.55 \\ 32.59$	24.80 25.04	
3	$C_9H_9N_3S$	Caled. Found	$\begin{array}{c} 56.54 \\ 56.32 \end{array}$	4.71 4.78	$21.98 \\ 21.80$	16.75 17.04	
4	$C_{10}H_{11}N_3S$	Calcd. Found	58.53 58.70	5.36 5.37	$20.48 \\ 20.55$	15.60 15.90	
5	$C_{11}H_{13}N_3S$	Calcd. Found	60.27 60.04	5.93 5.93	19.17 19.32	14.61 14.87	
6	$C_{12}H_{15}N_3S$	Calcd. Found	$61.82 \\ 61.78$	6.43 6.42	18.02 17.96	13.73 14.01	
7	$C_4H_7N_3S$	Calcd.	37.22	5.42	32.55	24.80	

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Table IV (continued) Microanalytical Data of the Compounds Listed in Table III

Compound	Empirical	Elemental Analysis (%)						
No.	Formula		C	Н	N	S		
0		Found	37.18	5.46	32.52	24.89		
8	$C_8H_{15}N_3S$	Caled.	51.89	8.10	22.70	17.29		
0		Found	51.86	8.17	22.68	17.35		
9	$C_6H_{11}N_3S$	Calcd.	45.85	7.00	26.75	20.38		
10	$C_7H_{13}N_3S$	Found	45.75	7.08	26.78	20.39		
10		Calcd.	49.12	7.60	24.56	18.71		
11	$C_8H_{15}N_3S$	Found	49.10	7.63	24.63	18.70		
**		Calcd.	51.89	8.10	22.70	17.29		
12	C ₉ H ₉ N ₃ O	Found	51.76	8.26	22.80	17.20		
12		Caled.	61.71	5.14	24.00			
13	C II N O	Found	61.60	5.35	24.00			
15	$C_{10}H_{11}N_3O$	Caled.	63.49	5.82	22.22			
14	C II N O	Found	63.44	5.88	22.38			
	$C_{11}H_{13}N_3O$	Calcd.	65.02	6.40	20.68			
45		Found	64.89	6.44	20.81			

66.35

65.64

Calcd.

Found

REFERENCES AND NOTES

19.35

19.48

General Synthesis of 3-Hydroxy- and 3-Mercapto-1,2,4-triazoles.

 $C_{12}H_{15}N_3O$

The following preparation of 3-mercapto-5-methyl-1,2,4-triazole (Table III, Experiment No. 1) will serve as an example of the procedure used to prepare compounds listed in Table III. In this case thiosemicarbazide (0.91 g., 0.01 mole) was dissolved in anhydrous methanol and $1.51~\mathrm{g}$. (0.01 mole) of methyl selenonester in 10 ml. of anhydrous methanol was added. The mixture was heated under reflux for 48 hours, then the suspension which resulted was filtered. The filtrate was evaporated leaving 0.8 g. (70%) of product, m.p. 216°.

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