

SYNTHESIS OF SELENAZOLO[3,2-b] [1,2,4] TRIAZINE AND SELENAZOLO [2,3-c] [1,2,4] TRIAZINE

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Abstract

6-Methyl-1,2,4-triazine-3-(2H)-selenone-5(4H)-one (1) reacts in the presence of base with phenacyl bromide to give a mixture of compounds (2) and (3). This mixture is dehydrated in the presence of H_2SO_4 to give 3-phenyl-6-methyl-7H-selenazolo[3,2-b] [1,2,4] triazin-7-one (6). For careful structure assignment of (6) its regioisomer 3-methyl-6-phenyl-4H-selenazolo [2,3-c] [1,2,4] triazin-4-one (8) was unambiguously synthesized and its spectroscopic data were compared with those of (6).

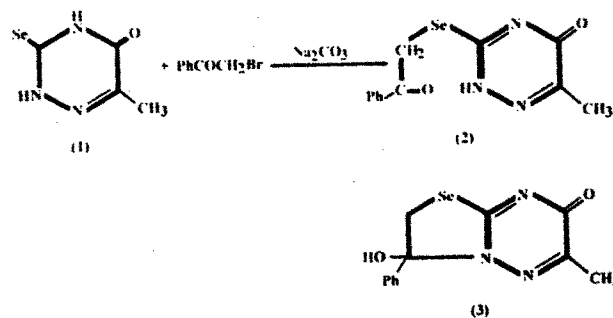
Introduction

In spite of the interest shown in the synthesis of bicyclic compounds derived from 1,2,4-triazine [1] and heterocycles containing selenium [2], a literature survey revealed only one reference concerning the synthesis of selenazolo-1,2,4-triazine [3]. Due to the wide range of physiological activities of compounds containing a triazine ring [4-7], and heterocycles containing selenium [8,9] this study was deemed worthwhile.

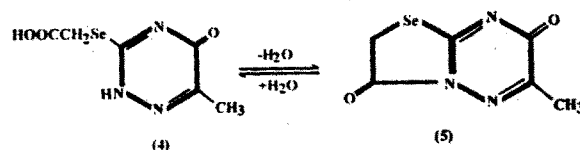
Results and Discussion

As part of our interest in the chemistry of bicyclic compounds derived from 1,2,4 triazine [10-12], 6-methyl 1,2,4-triazine-3(2H) selenone-5(4H)-one (1) [3] was reacted with phenacyl bromide in the presence of sodium carbonate to obtain compound (2). The IR spectrum of this compound showed amide carbonyl at 1630 cm^{-1} and keto carbonyl at 1700 cm^{-1} . Mass spectrum showed M^+ at m/e 308 due to either condensed (2) or cyclized (3) compound. 1H NMR of the obtained compound clearly showed two different methyl and methylene groups due to condensed (2) and cyclized (3) compound. When the time and temperature of reaction increased, the same result was obtained. Therefore, we could assume that in basic solutions

3-phenacylseleno 6-methyl-1,2,4-triazin-5(2H)-one (2) is in equilibrium with 2-[H]-3 hydroxy-3-phenyl-6-methyl-7H-selenazolo[3,2-b] [1,2,4] triazin-7-one (3).



This phenomenon has also been observed in the ring closure of (4) to (5) [3]. However, when a mixture of (2)

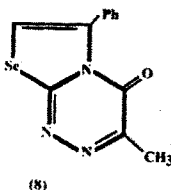
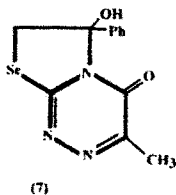
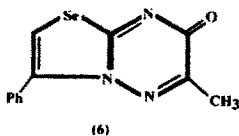


and (3) was refluxed in 20% H_2SO_4 a single crystalline compound was obtained which was identified as 3-phenyl-6-methyl-7H-selenazolo [3,2-b] [1,2,4] triazin-7-one (6).

Compound (2) can potentially cyclize on N_4 to give a

Keywords: Synthesis; Selenazolo as triazine

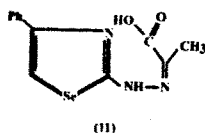
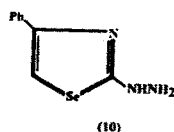
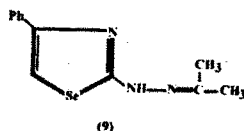
mixture of (2) and 7-[H]-6-hydroxy-3-methyl-6-phenyl-4H-selenazolo [2,3-c] [1,2,4] triazine-4-one (7). Dehydration of (7) with H_2SO_4 should give 3-methyl-6-phenyl-4H-selenazolo [2,3-c] [1,2,4] triazin-4-one (8).



Both the exclusive cyclization on the N-2 nitrogen atom and cyclization on N-4 are reminiscent of the alkylation of 3-methyl-mercapto 1,2,4-triazin-5(2H)-ones with alkyl halides under basic conditions. Alkylation of the latter with CH_3I in the presence of base provides only N-2 alkylation product while in the case of 6-phenyl derivative a mixture of N-2 and N-4 alkylation product is obtained in a 4:1 ratio [13, 14].

For definite structure assignment of (4) and to obtain a new heterocyclic system it was decided to synthesize (8) unambiguously.

2[4-Phenylselenazolyl] hydrazone of acetone (9) [15] was prepared from the reaction of selenosemicarbozone of acetone and phenacyl bromide, we could not repeat Bulka's procedure [15] for acid hydrolysis of (9) to 2-hydrazino-4-phenylselenazole (10). However (9) was successfully converted to (10) by refluxing in hydrazine hydrate. Reaction of (10) with pyruvic acid gave 2[4-(phenyl selenazolyl)] hydrazone of pyruvic acid (11). The latter was refluxed in glacial acetic acid for 6 h to afford (8). Structures (6) and (8) were distinguished from their physical and spectral data. The UV spectra of (8) with a dienone structure shows the absorption maxima at the longer wavelength compared to (6) with a quinone structure. We could therefore conclude that the reaction of (1) with α -haloketones proceeds via cyclization on N-2 of 1,2,4 triazine and exclusively affords (6).



Experimental Section

The melting points are uncorrected and were obtained by a Kofler Heizbank Richert type 7841 melting point apparatus. IR spectra were obtained on a 4300 Shimadzu spectrometer. The 1H NMR spectra were recorded on a Varian 50 A spectrometer using TMS as internal reference and mass spectra were scanned on a Varian Mat CH-7 instrument at 70 eV.

Reaction of (1) with Phenacyl Bromide

Compound 1 (0.19 g; 0.001 mol) was dissolved in sodium carbonate solution [sodium carbonate (1 g) in water (10 mL)]. To this stirred solution phenacyl bromide (0.199 g; 0.001 mol) in ethanol (10 mL) was slowly added. The mixture was stirred at room temperature for 2 h.

The precipitated solid was filtered off to afford a mixture of 2 and 3, yield 0.12 g, 39%. 1H NMR $\delta(d_6$ -DMSO) 2.1 (s, 3H, Me of 3) 2.2 (s, 3H, Me of 2) 3.9 (s, 2H, CH_2 of 3), 4.9 (s, 2H, CH_2 of 2) 7.5-7.8 (m, 10H, 2Ph), 8(s, 1H, OH). M^+ , m/e 308; IR (KBr disk) 3550 (OH), 1700 (ketone carbonyl) 1630 (amide carbonyl) cm^{-1} .

3-Phenyl-6-methyl-7H-selenazolo[3,2-b][1,2,4] triazin-7-one(6).

The above mixture (0.59 g, 1.9 mol) was refluxed in 20% sulphuric acid (5 mL) for 1 h. The solution was cooled down to room temperature, the solid was filtered and crystallized from H_2O to afford the title compound: yield 0.39 g, 70% m.p. 240° (decomp). 1H NMR: $\delta(d_6$ -DMSO), 2.0 (s, 3H, Me), 7.1-7.3 (m, 5H, Ph), 7.1 (s, 1H, CH), ms: m/z (rel. intensity) 290 (M^+ , 23) 288(11), 242(89), 240(40), 216(14), 180(11), 178(89), 176(40), 118(14), 102(44), 99(100), 87(14), 76(55), 50(33); IR (KBr disk): 1635 amid carbonyls; uv (DMSO) λ_{max} 250 nm(1.143) 278(1.09).

2-Hydrazino-4-phenylselenazole(10)

Compound 9 (0.56 g, 0.002 mol) was dissolved in EtOH (20 mL). To this solution, hydrazine hydrate (0.2 g, 0.004 mol) was added. The reaction mixture was refluxed for 20 min. The solution was cooled down to room temperature and the solid was filtered off to afford the title compound: yield, 30%, m.p. 150° [lit 15, m.p. 145°]; 1H NMR, $\delta(d_6$ -DMSO) 5.0 (s, 2H, NH_2), 7.1 (s, 1H, CH) 7.2-7.6 (m, 5H, Ph), 7.8 (s, 1H, NH), ms: m/e, (rel. intensity) 238 (M^+ 5.6), 236(23) 234(11), 138(17), 132(42), 55(28.5), 43(5.6), 42(28.5), 41(100), 31(57), 28(28.5).

2[4-Phenylselenazolyl] hydrazone of pyruvic acid(11)

Compound 10 (0.238 g, 0.001 mol) was dissolved in EtOH (20 mL). To this solution, pyruvic acid (0.088 g, 0.001 mol) was added. The reaction mixture was refluxed for 1 h. The solvent was evaporated off and the solid was collected to afford the title compound: yield 50%, m.p.

145-146°C, ¹H NMR (d₆-DMSO) 2.1 (s, 3H), 7.2 (s, 1H, CH), 7.3-7.7 (m, 5H, Ph), 7.8 (s, 1H, NH), m/s: m/e (%) 308(rel.intensity) 308(M⁺, 602), 307(37), 260(93), 258(46), 219(22), 218(18.75), 192(15.6), 186(12.5), 180(100), 176(12.5), 102(56), 50(9.3).

3-Methyl-6-phenyl-4H-selenazolo[2,3-c][1,2,4]triazin-4-one(8)

Compound 11 (0.30 g, 0.001 mol) was dissolved in glacial acetic acid (10 mL). The reaction mixture was refluxed for 6 h. The solvent was evaporated off to dryness and the solid was collected to afford the title compound: yield 70%, ¹H NMR δ(d₆-DMSO): 2.0 (s, 3H) 7.2 (s, 1H, CH), 7.5-7.7 (m, 5H, Ph), ms: m/e(%) 291(M⁺, 5), 290(1.5), 248(15), 118(65), 103(96), 75(100), 50(78), 44(43); IR (KBr disk) 1650 cm⁻¹ (amide carbonyl); uv (DMSO) λ_{max} nm, 258(1.07), 325(0.52).

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