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Base Catalyzed Cyclization and Isomerization of 3-Propargylseleno 1,2,4-Triazine to Selenazolo [3,2-b] [1,2,4] - Triazine

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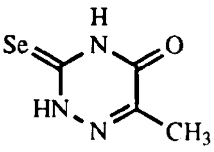
Summary: Transformation of 3-propargylseleno-6-methyl-1,2,4-triazin-5(2H)-one (2) to 3-methylene-2,3-dihydro-7H-selenazolo [3,2-b] [1,2,4] - triazin - 7- one (3) and 3,6 - dimethyl-7H selenazolo [3,2-b] [1,2,4] - triazine (4) is performed under the condition of Triethylamine and sodium methoxide respectively. The formation of 3 and 4 may be mainly due to the high reactivity of acetylenes towards nucleophiles. Compound 4 can be formed through isomerization of 3.

Introduction

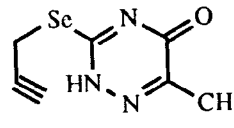
Since many compounds containing 1,2,4-triazine ring system have interesting pharmacological properties [1-4] selenazolo [3,2-b] [1,2,4] - triazine could be interesting from the view point of chemical reactivity and also biological activity.

Many efforts have been devoted to the synthesis of thiazolo [3,2-b] [1,2,4] - triazine [5-9]. However, there is only one reference in the literature reporting the synthesis of 6-phenyl-7H-selenazolo [3,2-b]-2,3-dihydro-[1,2,4] - triazine - 3,4-dione [10].

Here we wish to report a facile synthesis and aromatization of a novel aromatic system of selenazolo [3,2-b] - 1,2,4 - triazine.



(1)



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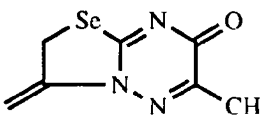

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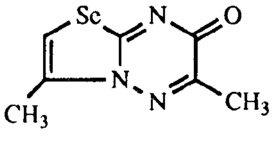

(4)

Results and Discussion

6-Methyl-3-seleno-1,2,4-triazin-5 (2H,4H)-one (**1**) [10] was condensed with propargyl bromide in the presence of sodium methoxide to afford 6-methyl-3-propargylseleno-1,2,4-triazin-5(2H)-one (**2**). When **2** was refluxed in a mixture of triethylamine and ethanol, a crude was obtained which was chromatographed over silica gel to afford mainly a crystalline compound. Based on spectral data, structure **3** was assinged to this compound. The olefinic protons in **3** appeared separated by *ca.* 0.6 ppm. When **2** was refluxed with sodium methoxide in MeOH for 4h, a solid was isolated, which was crystallized from ethanol to give a white crystalline compopund. The compound was identified as 3,6-dimethyl-7H-selenazolo [3,2-b] [1,2,4]-trazin-7-one (**4**).

Compound **4** was synthesized unambiguouslly through the reaction of **1** with bromoacetone in the presence of sodium carbonate and subsequent dehydration of hydroxy compound **5** scheme (1). By elucidation of structure, it can be assumed that the base abstracts a hydrogen from the nitrogen 2 of **2**. The nitrogen then attacks the acetylenic group to give the cyclized intermediate **3**. Isomerization of the intermediate produces compound **4** (scheme 2).

Alternatively **3** was converted to **4** by treatment with boiling $CH_3O^-Na^+/CH_3OH$

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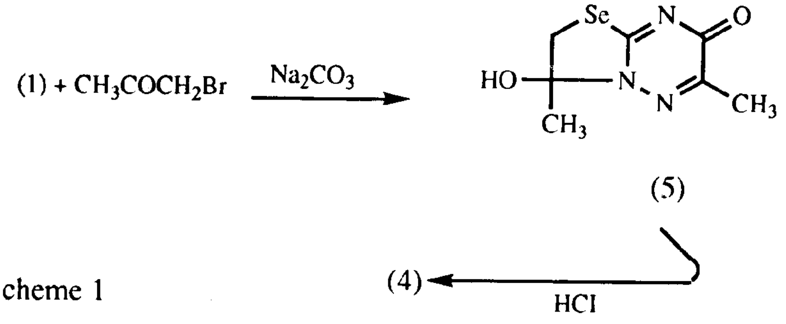
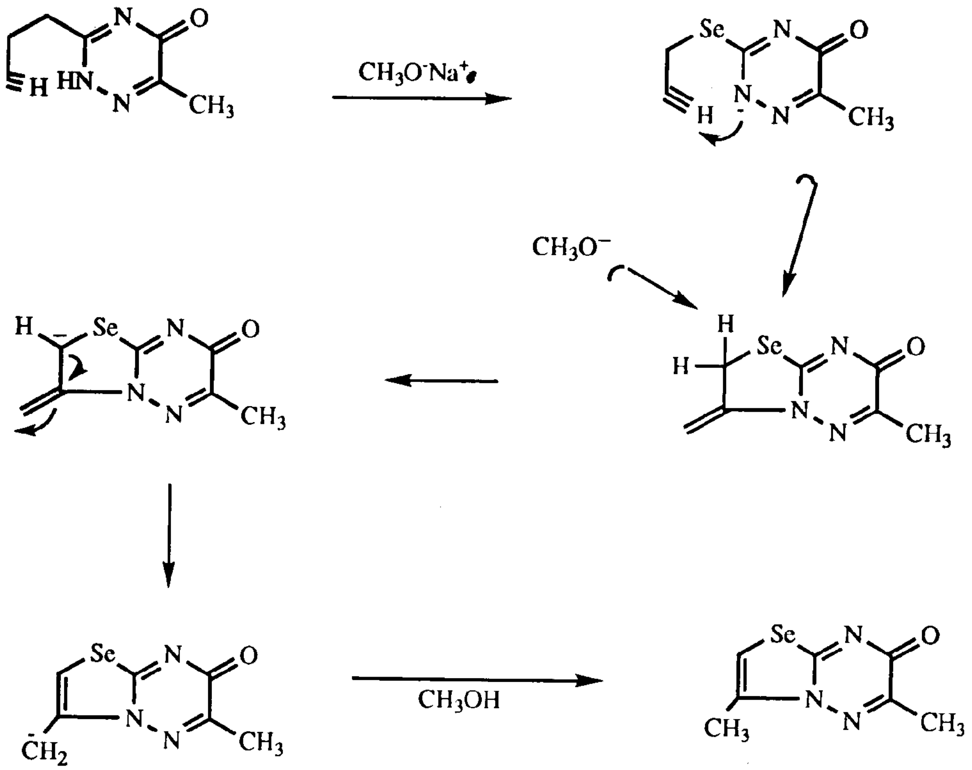


Scheme 1



Scheme 2

Experimental

Melting points (uncorrected) were obtained on a Thomas Hoover capillary melting points apparatus. The ^{1}H nuclear magnetic resonance (^{1}H-NMR) was obtained on a 300 MHzGE QE, with deuterodimethyl sulfoxide (DMSO-d_6) as solvent and internal standard. Infrared spectra (IR) were recorded on a Perkin-Elmer model 283 grating spectrophotometer using 0.1 mm NaCl plates. Mass spectra were obtained on a VG-ZAB at 70 ev.

*6-Methyl-3-propargylseleno-1,2,4-triazin-5(2H)-one (**2**)*

Sodium (1 g 0.043 mole) was dissolved in MeOH (100 ml). To this solution, compound **1** (5 g; 0.026 mol) was added. Under nitrogen, propargyl bromide (4.5 ml of 80% solution in toluene) was added dropwise at room temperature. The reaction mixture was stirred at ambient temperature for 4 h; The solid was filtered off, washed with water and crystallized from ethanol to afford the title compound. mp. 185-186°C, yield 5.2 g 86% (Anal. calcd. for $C_7H_7N_3OSe$, C, 37.21, H, 3.09: N, 18.42. Found: C, 37.11; H, 3.13; N, 18.32. IR (Nujol) $\lambda_{max}cm^{-1}$; 3450 (NH), 2262 (C≡C,w), 1630 (amide carbonyl): ^{1}H-NMR (DMSO-d_6), δ 2 (S, 3H, Me), 3(S,1H,CH), 4 (S, 2H, CH_2); ms: m/z 229 (M^+).

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

The compound **2** (1g; 0.004 mol) was added to the mixture of triethylamine (5 ml) in ethanol (30 ml). The reaction mixture was refluxed for 2h. The solvent was evaporated to dryness. The crude was subjected to column chromatography over silica gel using $CHCl_3$ as an eluent to obtain the title compound, mp. 190-191, yield 0.55 g, 55% (Anal. calcd. for $C_7H_7NO_3Se$, C, 37.21, H, 3.09; N, 18.92. Found: C, 37.01; H, 3.15; N, 18.37).' IR (Nujol),. λ cm^{-1}, 1630 (amide carbonyl); ^{1}H-NMR (DMSO-d_6), δ 2.1 (S, 3H, Me), 4.1 (S, 2H, CH_2), 4.82 (q, J = 2.2 Hz, 1H), 5.58 (q, J = 2.2, Hz); ms; m/z 229.

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

The compound 1 (1 g; 0.004 mol) was added to the solution of sodium methoxide in methanol (Na, 126 mg in MeOH 20 ml). The reaction mixture was refluxed for 4h. The solvent was evaporated off to dryness under reduced pressure. Water was added to the crude. The solid was filtered, washed with water and crystallized from EtOH. mp. 220-221°C; yield 0.8 g, 80%; (Anal. calcd. for $C_7H_7N_3OSe$, C, 37.21; H, 3.09, N, 18.42. Found: C, 37.05; H, 3.04; N, 18.55. IR (Nujol) λ cm^{-1}, 1630 (amide carbonyl). ^{1}H-NMR, (DMSO-d_6) δ 2.1 (S, 3H, Me), 2.3 (s, 3H, Me), 6.6 (S, 1H, CH, five membered ring); ms: m/z 229.

3,6-Dimethyl-3-hydroxy-2,3-dihydro-7H-selenazalo [3,2-b] [1,2,4] - triazin-7-one (5).

The compound **1** (1 g; 0.004 mol) was dissolved in carbonate solution [sodium carbonate (2g) in water (25 ml)]. To this solution, bromoacetone (0.68 g, 0.005 mol) in ethanol was added dropwise. The reaction mixture was stirred at ambient temperature for 1h. The solid was filtered off, washed thoroughly with water and crystallized from EtOH to afford the title compound: mp. 208-209°C; yield 1.05 g; 81%; (Anal. calcd. for $C_7H_9N_3O_2Se$, C, 34.16; H, 3.68, N, 17.07. Found: C, 34.31; H, 3.56; N, 17.23) IR (Nujol) λcm^{-1}, 1630 (amide carbonyl) ^{1}H-NMR (DMSO-d_6) δ 2.1 (S, 3H, Me), 2.3 (S, 3H, Me), 3.8 (S, 2H, CH_2); ms: m/z 247.

Treatment of 3,6-dimethyl-3-hydroxy-2,3-dihydro-7H-selenazolo [3,2-b] [1,24] - triazin-7H-one with hydrochloric acid.

Compound **5** (0.5 g; 0.002 mol) was refluxed in conc. hydrochloric acid (20 ml) for 1 h. The solution was cooled down to -5°C. The white solid was filtered off, washed with sodium carbonate solution (10%) to afford the compound which was identical to 4: mp. 222-223°C; yield, 3 g, 65%.

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