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Received August 30, 1982

Diazotized anthranilic acid and its methyl ester react with ethyl  $\alpha$ -selenocyanatoacetate **3a** and  $\alpha$ -selenocyanatoacetoacetanilide **3b** to give in both cases the corresponding 1,3,4-selenadiazolo[2,3-*b*]quinazoline derivatives **7a** and **7b**, respectively, in good yields (70-80%). A mechanism is proposed and it is substantiated by an alternate synthesis of **7a** and **7b** from the corresponding hydrazidoyl chlorides **9a** and **9b** with potassium selenocyanate, respectively. An evidence for the involvement of the 1,3,4-selenadiazoline derivative as an intermediate in these reactions is provided by the isolation of **11** from either coupling of **3b** with diazotized ethyl *p*-aminobenzoate or the reaction of hydrazidoyl chloride **12** with potassium selenocyanate.

*J. Heterocyclic Chem.*, **20**, 719 (1983).

The Japp-Klingemann reaction of active methine compounds **1** with arenediazonium salts to give the monoarylhydrazones **2** (equation 1) is a long known process (2). Although numerous active methine compounds have been used in this reaction no information is available on the use of selenocyanates **3**. We now report an investigation of the use of this reaction in the synthesis of the title compounds from **3a-b** and diazotized anthranilic acid or its methyl ester (Scheme 1). The 1,3,4-selenadiazolo[2,3-*b*]quinazoline ring system has not previously been reported.

### Results and Discussion.

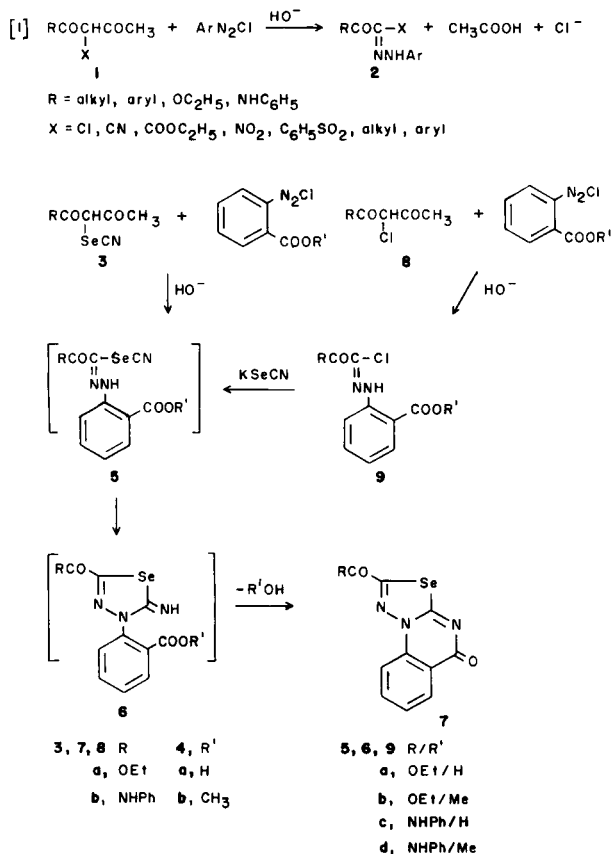
The reaction of ethyl  $\alpha$ -selenocyanatoacetoacetate **3a** with diazotized anthranilic acid **4a** in ethanolic sodium acetate buffered solution after work up and purification gave a colored product, C<sub>12</sub>H<sub>9</sub>N<sub>3</sub>O<sub>3</sub>Se. The infrared spectrum of this compound was free of bands due to free selenocyanato (2160 cm<sup>-1</sup>), hydrazone NH (3340 cm<sup>-1</sup>) and carboxylic OH (3100-2850 cm<sup>-1</sup>) groups. It revealed, however, the presence of two carbonyl bands near 1680 and 1715 cm<sup>-1</sup>. Based on these data, the product obtained was assigned the 1,3,4-selenadiazolo[2,3-*b*]quinazoline structure **7a** (Scheme 1). This assignment was supported by our finding that **7a** was also obtained from coupling of **3a** with diazotized methyl anthranilate **4b** in ethanol in the presence of sodium acetate (Scheme 1).

Similarly, treatment of  $\alpha$ -selenocyanatoacetoacetanilide **3b** with diazotized anthranilic acid or its methyl ester gave in both cases one product identified as **7b**.

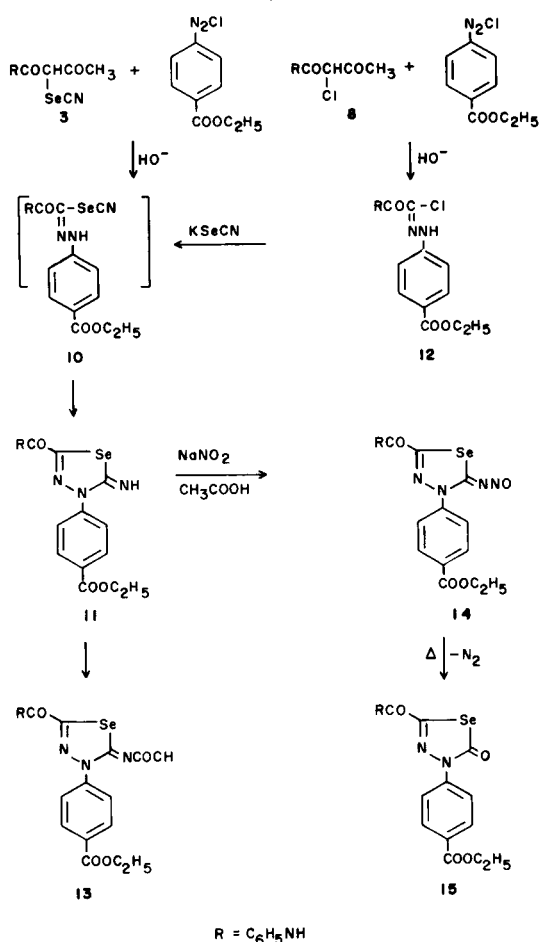
The structures of **7a** and **7b** were substantiated further by alternate synthesis. Thus, treatment of the hydrazidoyl chlorides **9a-b** and **9c-d** with potassium selenocyanate in refluxing ethanol yielded products identical in all respects (mp, mixed mp, ir, and pmr) with **7a** and **7b**, respectively (Scheme 1).

The most compatible mechanism that can account for such findings is presented in Scheme 1. It is thought that **3** undergoes first Japp-Klingemann reaction to give **5**. The latter undergoes spontaneous cyclization to yield the iminoselenadiazoline derivative **6**, which completes the reaction by the loss of the elements of water (in case of **6a** and **6c**) or methanol (in case of **6b** and **6d**) to afford the final product **7**. The direct cyclization of **5** into **6** is analogous to the behaviour of  $\alpha$ -thiocyanatohydrazones which were reported to undergo cyclization once they are formed from hydrazidoyl halides and potassium thiocyanate or from coupling of phenacylthiocyanate with diazotized aromatic amines (3). In our hands, all attempts to isolate the intermediates **5** and **6** were unsuccessful.

Scheme 1



Scheme 2



To substantiate the involvement of **6** as intermediate in the studied reactions coupling of **3b** with diazotized ethyl *p*-aminobenzoate in ethanol in the presence of sodium acetate was investigated. Under such conditions, the product obtained was identified as the 1,3,4-selenadiazoline derivative **11**. The structure of the latter product **11** was supported by its spectral and elemental analysis data and its chemical behaviour summarized in Scheme 2. In the ir spectrum, **11** had bands due to imino NH (3225 cm<sup>-1</sup>) and carbonyl groups (1740, 1680 cm<sup>-1</sup>). In the pmr spectrum **11** revealed signals at  $\delta$  1.3 (t, 3H, J = 7.0 Hz), 4.1 (q, 2H, J = 7.0 Hz) and a multiplet in the 7.0-8.2 ppm region. The structure of **11** was also confirmed by its alternate synthesis from the hydrazidoyl chloride **12** and potassium selenocyanate (Scheme 2). Nitrosation of **11** with sodium nitrite in acetic acid yielded the *N*-nitroso derivative **14**, which upon thermolysis in xylene gave the corresponding selenadiazolone derivative **15**. Acetylation of **11** with acetic anhydride yielded the *N*-acetyl derivative **13**. The spectral data and the satisfactory elemental analyses of the products **13-15** were consistent with their assigned structures (see Experimental).

The foregoing results indicate that coupling of  $\alpha$ -selenocyanato derivatives of active methylene compounds with diazotized anthranilic acid or its methyl ester seems to be an efficient and rapid experimental procedure for synthesis of selenadiazolo[2,3-*b*]quinazolines derivatives.

## EXPERIMENTAL

Proton magnetic resonance spectra were recorded on Varian T60-A spectrometer using tetramethylsilane as an internal standard. Infrared spectra were obtained on Perkin Elmer 257 grating spectrophotometer. Mass spectra were recorded on a Perkin Elmer RMU-6E spectrometer with ionization energy of 70 eV. Melting points were obtained on a Thomas-Hoover capillary tube melting point apparatus and are uncorrected. Elemental analyses were carried out at the Microanalysis Laboratory of the University of Cairo, Egypt.

Ethyl  $\alpha$ -chloroacetoacetate (**4**),  $\alpha$ -chloroacetoacetanilide (**5**), ethyl  $\alpha$ -selenocyanatoacetoacetate (**6**) and  $\alpha$ -selenocyanatoacetoacetanilide were prepared as previously described.

Preparation of Hydrazidoyl Chlorides **9a-d** and **12**, General Procedure.

To a cold solution of ethyl  $\alpha$ -chloroacetoacetate **8a** (or  $\alpha$ -chloroacetoacetanilide **8b**) (0.01 mole) and sodium acetate (1.3 g) in ethanol (50 ml) was added dropwise while stirring a solution of the appropriate diazonium salt of anthranilic acid (methyl anthranilate or ethyl *p*-aminobenzoate) (0.01 mole). Stirring was continued for 1 hour after addition was complete, and the mixture was left overnight in ice box. The crude product which precipitated was collected and crystallized from ethanol.

Compound **9a**.

This compound had mp 221° (lit (4) mp 216°).

Compound **9b**.

This compound had mp 104°.

Anal. Calcd. for C<sub>12</sub>H<sub>13</sub>ClN<sub>2</sub>O<sub>4</sub>: C, 50.60; H, 4.60; N, 9.84; Cl, 12.45. Found: C, 50.41; H, 4.50; N, 9.77; Cl, 12.33.

Compound **9c**.

This compound had mp 211° (lit (5) mp 216°).

Compound **9d**.

This compound had mp 153°.

Anal. Calcd. for C<sub>16</sub>H<sub>14</sub>ClN<sub>3</sub>O<sub>3</sub>: C, 57.93; H, 4.25; N, 12.66; Cl, 10.69. Found: C, 57.82; H, 4.11; N, 12.45; Cl, 10.60.

Compound **12**.

This compound had mp 194°.

Anal. Calcd. for C<sub>17</sub>H<sub>16</sub>ClN<sub>3</sub>O<sub>3</sub>: C, 59.05; H, 4.66; N, 12.15; Cl, 10.25. Found: C, 59.10; H, 4.44; N, 12.22; Cl, 10.10.

Selenadiazolo[2,3-*b*]quinazolines **7a-b**. Method A.

To a cold solution of ethyl  $\alpha$ -selenocyanatoacetoacetate **3a** (or  $\alpha$ -selenocyanatoacetoacetanilide **3b**) (0.01 mole) and sodium acetate (1.3 g) in ethanol (50 ml) was added dropwise a solution of diazotized anthranilic acid **4a** (or methyl anthranilate **4b**) (0.01 mole) while stirring. The addition took 30 minutes, after which stirring was continued for 3 hours. The solid that precipitated was collected, washed with water and crystallized from dimethylformamide.

Compound **7a**.

This compound had mp 194°.

Anal. Calcd. for C<sub>12</sub>H<sub>9</sub>N<sub>3</sub>O<sub>3</sub>Se: C, 44.74; H, 2.82; N, 13.04. Found: C, 44.64; H, 2.75; N, 13.10.

Compound **7b**.

This compound had mp 239-240°.

Anal. Calcd. for C<sub>16</sub>H<sub>10</sub>N<sub>4</sub>O<sub>2</sub>Se: C, 52.04; H, 2.73; N, 15.17. Found: C,

52.00; H, 2.69; N, 15.20.

#### Method B.

To a suspension of **9** (0.005 mole) in ethanol (30 ml) potassium selenocyanate (0.7 g) was added. The mixture was refluxed for 15 minutes and cooled. The crude product was collected and crystallized from dimethylformamide. The product obtained from **9a** and **9b** was identical in all respects (mp, mixed mp, ir and pmr) with **7a**. Similarly **9c** and **9d** yielded one product identical with **7b**.

#### Preparation of **11**.

This was prepared from **3b** and diazotized ethyl *p*-aminobenzoate (Method A) and from **12** and potassium selenocyanate (Method B) following the same procedures described for synthesis of **7a-b**. Crystallization of the crude product obtained from either method, from ethanol gave **11**, (70-80% yield), mp 148°.

*Anal.* Calcd. for  $C_{18}H_{16}N_4O_3Se$ : C, 52.06; H, 3.88; N, 13.49. Found: C, 52.10; H, 3.75; N, 13.35.

#### Acetylation of **11**.

Compound **11** (0.5 g) was refluxed in acetic anhydride (10 ml) for 20 minutes and the mixture was cooled and poured on crushed ice. The crude *N*-acetyl derivative was collected and crystallized from acetic acid to give **13** in almost quantitative yield, mp 183°; pmr (deuteriochloroform):  $\delta$  1.3 (t, 3H), 2.3 (s, 3H), 4.1 (q, 2H); 6.9-8.2 (m, 10H).

*Anal.* Calcd. for  $C_{20}H_{18}N_4O_4Se$ : C, 52.52; H, 3.97; N, 12.25. Found: C, 52.41; H, 3.85; N, 12.21.

#### Nitrosation of **11**.

To a stirred solution of **11** (1.0 mmole) in acetic acid (10 ml), an

aqueous solution of sodium nitrite (140 mg, 2.0 mmoles) was added, dropwise at room temperature. After 1 hour, a small amount of water was added to the reaction mixture and the reddish product, thus precipitated, was collected, washed with water and crystallized from acetic acid. Compound **14** (yield 75%) had mp 110° dec.

*Anal.* Calcd. for  $C_{18}H_{15}N_3O_4Se$ : C, 48.60; H, 3.40; N, 15.76. Found: C, 48.51; H, 3.31; N, 15.65.

#### Thermolysis of **14**.

Compound **14** (0.3 g) was refluxed in xylene (30 ml). After 1 hour, the solvent was distilled off and the residue was triturated with petroleum ether (40/60) and the solid formed was collected and crystallized from ethanol to give **15** (95% yield), mp 160°.

*Anal.* Calcd. for  $C_{18}H_{15}N_3O_4Se$ : C, 51.93; H, 3.63; N, 10.12. Found: C, 51.82; H, 3.55; N, 10.12.

## REFERENCES AND NOTES

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