Preparation of 4,5-Dihydro-1,3-selenazoles by Reaction of Aromatic Primary Selenoamides with Acetylenedicarboxylate

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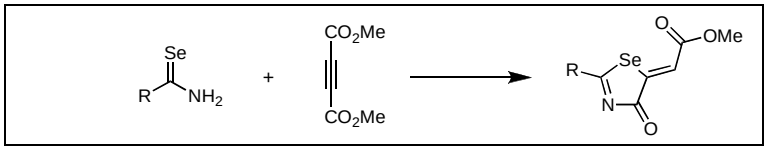
Received March 10, 2006



Reactions of primary selenoamides with dimethyl acetylenedicarboxylate afforded 2-aryl-5-methoxycarbonylmethylene-4,5-dihydro-1,3-selenazol-4-ones in moderate to high yields. Reactions of the primary selenoamides with acetylenedicarboxylic acid gave 2-aryl-5-carboxymethylene-4-ethoxy-4,5-dihydro-1,3-selenazol-4-ols in moderate yields.

J. Heterocyclic Chem., **44**, 231 (2007).

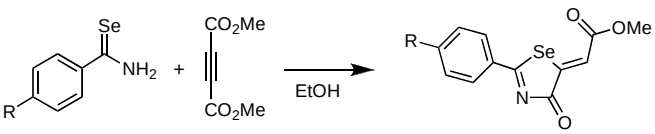
INTRODUCTION

Many syntheses of selenium-containing heterocyclic compounds have been reported because of their interesting reactivities [1]. Recently, the synthesis of selenium heterocycles has been extensively studied using the carbon-selenium double bond as 2π dienophile intermediates for [4+2] cycloadditions. For example, α,β-unsaturated selenoaldehydes and selenoketones selectively undergo 'head-to-head' [4+2] dimerization to give six-membered cyclic diselenides [2]. The reaction of selenoazadiene with dimethyl acetylenedicarboxylate (DMAD) affords a 4*H*-selenazine, six-membered ring compound, that converts to a 4*H*-selenopyran by cycloreversion and recycloaddition with excess DMAD [3]. Furthermore, six-membered ring, 2-iminoperhydro-1,3-selenazin-4-ones are synthesized by the reaction of *N*,*N*'-disubstituted selenoureas with acryloyl chloride [4]. On the other hand, five-membered ring 1,3-selenazolin-4-ones are obtained by a cycloaddition and intramolecular substitution between selenoazadiene and DMAD [5]. Thus, utility of the compounds bearing carbon-selenium double bond as 2π dienophile such as selenoamides, selenourea and selenazadienes could supply prospects for a variety of selenium-containing heterocycles [6]. Herein, we describe the syntheses of 2-aryl-5-methoxycarbonylmethylene-4,5-dihydro-1,3-selenazol-4-ones using aromatic primary selenoamides.

RESULTS AND DISCUSSION

Primary selenoamides (**1a-1d**) were prepared by previous reported method [7]. Dimethyl acetylenedicarboxylate (DMAD) (**2**) was added to a solution of 4-methylselenobenzamide (**1b**) in anhydrous methanol and stirred at room temperature for 15 min. 5-Methoxycarbonylmethylene-2-(4-methylphenyl)-4,5-dihydro-1,3-selenazol-4-one (**3b**) was obtained in 77% yield after recrystallization.

Scheme 1



1 **2** **3**

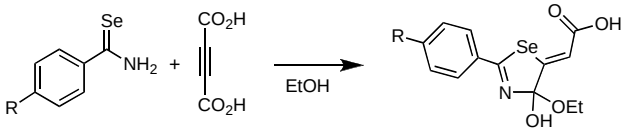
R	Yield (%)
CH_3O	91 (**3a**)
CH_3	57 (**3b**)
CH_3	77 (**3b**)*
H	61 (**3c**)
Cl	62 (**3d**)

*: MeOH was used.

The structure of 5-methoxycarbonylmethylene-2-(4-methylphenyl)-1,3-selenazolin-4-one (**3b**) was fully characterized. Four other 2-aryl-5-methoxycarbonylmethylene-4,5-dihydro-1,3-selenazol-4-ones (**3**) were prepared by reactions of primary selenoamides **1** with DMAD (**2**) in moderate to high yields (Scheme 1). In the case of **3b**, reaction in methanol gave **3b** in higher yield (77 %) compared with reaction in ethanol (yield: 57 %).

Next, reactions of (**1**) with acetylenedicarboxylic acid (**4**) were studied. The reaction afforded 2-aryl-5-carboxymethylene-4-ethoxy-4,5-dihydro-1,3-selenazol-4-ols (**5**) in moderate yields. In this case, the ethoxy group at C4 position was introduced by the nucleophilic addition of oxygen of ethanol solvent (Scheme 2). Under these conditions, compound **5a** did not afford the desired product.

Scheme 2



1 **4** **5**

R	Yield (%)
CH_3O	0 (**5a**)
CH_3	53 (**5b**)
H	52 (**5c**)
Cl	34 (**5d**)

Hence, we described preparation of 4,5-dihydro-1,3-selenazole derivatives by the reactions of primary selenoamides (**1**) with acetylene dicarboxylate without any catalyst.

EXPERIMENTAL

Typical Procedure for Synthesis of 5-Methoxycarbonylmethylene-2-(4-methoxyphenyl)-4,5-dihydro-1,3-selenazol-4-one (3a). Dimethyl acetylenedicarboxylate (**2**) (74.4 μL, 0.60 mmol) in anhydrous ethanol (6.0 mL) was added to a stirred solution of 4-methoxyselenobenzamide (**1a**) (128 mg, 0.60 mmol) in ethanol (6.0 mL). The reaction mixture was stirred at room temperature for 15 min. Reaction mixture was dried over sodium sulfate and evaporated to dryness. Yellow solid (**3a**) (178 mg, Yield: 91%) was isolated by recrystallization (*n*-hexane). Mp 224.5-225.0ºC, IR (KBr): 1167, 1493, 1697 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ 3.91 (s, 3H, CH_3), 3.94 (s, 3H, CH_3), 7.05 (d, J = 8.8 Hz, 2H, Ar), 7.37 (s, 1H, =CH), 8.11 (d, J = 8.8 Hz, 2H, Ar); ^{13}C NMR (125 MHz, $CDCl_3$): δ 53.0, 55.9, 114.9, 124.2, 130.9, 132.4, 147.7, 166.2, 166.9, 184.7, 191.1; MS (FAB): m/z = 326 [M^++1].

5-Methoxycarbonylmethylene-2-(4-methylphenyl)-4,5-dihydro-1,3-selenazol-4-one (3b). Orange crystals. Mp: 220.5-221.5ºC, IR (KBr): 1165, 1523, 1694 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 2.48 (s, 3H, CH_3), 3.91 (s, 3H, CH_3), 7.37 (m, 3H, Ar and =CH), 8.03 (d, J = 8.2 Hz, 2H, Ar); ^{13}C NMR (125 MHz, $CDCl_3$): δ 22.0, 53.0, 124.7, 129.8, 130.1, 131.2, 147.2, 147.7, 166.7, 184.7, 192.6; ^{77}Se NMR (95 MHz, $CDCl_3$): δ 568.8; MS (EI): m/z = 309 [M^+].

Typical Procedure for 5-Carboxymethylene-4-ethoxy-2-(4-methylphenyl)-4,5-dihydro-1,3-selenazol-4-ol (5b). Acetylenedicarboxylic acid (**4**) (23.2 mg, 0.20 mmol) and 4-methylselenobenzamide (**1b**) (39.6 mg, 0.20 mmol) was added to anhydrous ethanol (2.0 mL). The reaction mixture was stirred at room temperature for 1.5 h. Reaction mixture was dried over sodium sulfate and evaporated to dryness. Yellow solid (**5b**) (36.4 mg, Yield: 53%) was isolated by recrystallization (*n*-hexane). Mp: 182.3-183.5ºC, IR (KBr): 1202, 1683, 2984, 3153 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ 1.22 (t, J = 7.2 Hz, 3H, OCH_2CH_3), 2.31 (s, 3H, CH_3), 3.50 (m, 1H, OCH_2CH_3), 3.58 (m, 1H, OCH_2CH_3), 7.03 (s, 1H, =CH), 7.20 (d, J = 8.0 Hz, 2H, Ar), 7.37 (d, J = 8.0 Hz, 2H, Ar), 10.2 (s, 1H, OH), 13.1 (brs, 1H, CO*OH*); ^{13}C NMR (125 MHz, DMSO-d_6): δ 14.6, 20.7, 59.8, 94.5, 117.2, 124.7, 129.0, 137.8, 139.9, 148.2, 167.8, 168.0; ^{77}Se NMR (95 MHz, DMSO-d_6): δ 563.8; MS (EI): m/z = 341 [M^+].

Acknowledgements. This work was supported by a Grant-in-Aid for Science Research from the Ministry of Education, Culture, Sports, Science and Technology of Japan (No. 15550030 and 17550099) to which we are grateful.

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