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The Synthesis of Bis(carboxyalkylmethyl) Diselenides by Selenium Transfer Reaction of Aryl Selenoamides

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Abstract: Aryl selenoamides react smoothly with α-haloacetic acid in various alcohol to give corresponding bis(carboxyalkylmethyl) diselenides in good yields.

Keywords: Aryl selenoamides, α-haloacetic acid, bis(carboxyalkylmethyl) diselenides, synthesis.

Aryl selenoamides are important intermediates in the synthesis of selenium–nitrogen heterocycles, moreover they can be expected to react with various organic or inorganic reagents owing to high reactivity of their carbon-selenium double bond[1, 2]. We have reported that primary selenoamides could be used as selenium transfer reagents in the synthesis of dialkyl diselenides from reactive halides[3] and diacyl selenides from acyl chlorides[4]. In continuation of our interest in the selenium transfer reaction of selenoamides, we treated biprotic selenoamides with functionalized α-haloacetic acid in 1:1 or 1:2 molar ratio in various alcohol and found that the reaction in different molar ratio furnishes the same C-Se-Se-C coupled products bis(carboxyalkylmethyl) diselenides **4a~e** (**Scheme 1**).

The results are shown in **Table 1** and all products were characterized by IR, ^{1}H NMR, MS and elemental analysis[5].

In order to investigate the mechanism, we selected methyl α-bromoacetate as startinng material and it was added to the solution of selenobenzoamide in ethanol at room temperature under the neutral condition. After the mixted solution was stirred for 5 h, the product bis(carboxyalkylmethyl) diselenides was obtained in high yield. Byproduct ethyl benzoate was also separated.

The results suggest that this C-Se-Se-C coupling reaction might be carried out as shown in **Scheme 2**. α-Haloacetic acid was at first esterified with alchol to form alkyl α-haloacetates and then bipronic selenoamides attacked the esters to undergo selenium transfer reaction. Bis(carboxyalkylmethyl) diselenides were therefore achieved *via* intermediates **5** and **6**.

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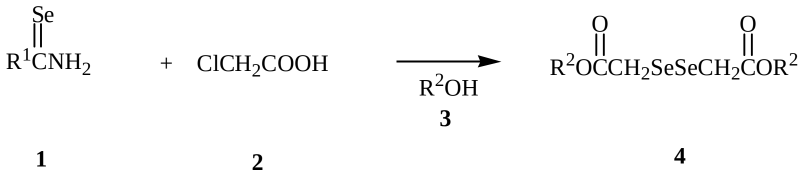
Scheme 1



Scheme 2

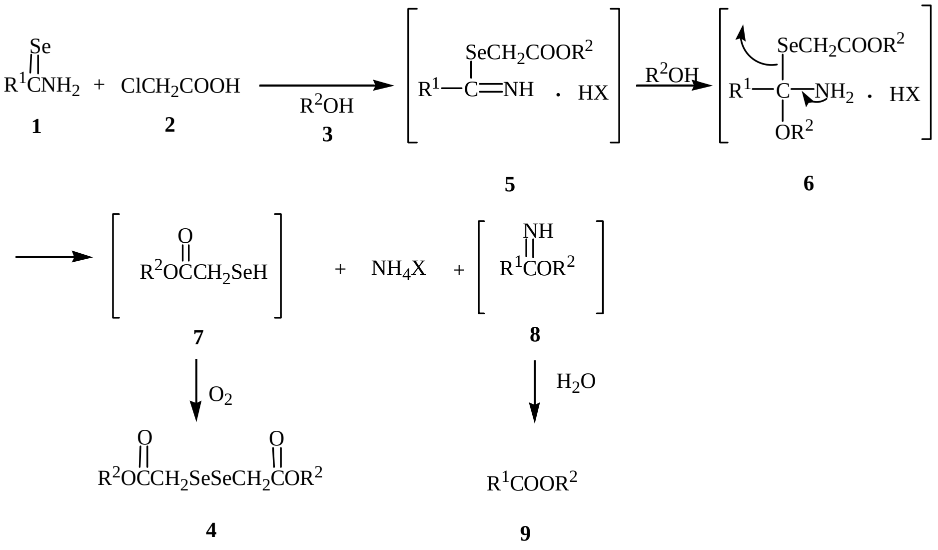


Table 1 Synthesis of bis(carboxyalkylmethyl) diselenides

Entry	R^1	R^2	**1/2**	Product	React. temp. (℃)	React. time (h)	Isolated yield (%)
1	C_6H_5	CH_3	1:1	**4a**	R.T.	4	88
2	C_6H_5	CH_3	1:2	**4a**	R.T.	3.5	91
3	C_6H_5	C_2H_5	1:1	**4b**	R.T.	4	90
4	3-MeC_6H_4	C_2H_5	1:1	**4b**	R.T.	4	91
5	C_6H_5	C_2H_5	1:2	**4b**	R.T.	3.5	93
6	C_6H_5	*i*-C_3H_7	1:1	**4c**	R.T.	10	78
7	C_6H_5	*n*-C_4H_9	1:1	**4d**	70	3	81
8	C_6H_5	*n*-C_3H_7	1:1	**4e**	50	3	86
9	C_6H_5	$C_6H_4CH_2$	1:1		120	8	-
10	C_6H_5	allyl	1:1		120	8	-

The literature reported that bis(carboxyalkylmethyl) diselenides have been synthesized by treatment of ethyl choloacetate with lithium diselenide[6], oxidation of potassium selenosulphate with I_2[7]. Bis(carboxyethylmethyl) diselenides was also achieved as byproduct of photoreductive reaction of phenylselenoalkane[8]. We provide a new and facile method for synthesis of bis(carboxyalkylmethyl) diselenides with the advantages of easily available starting materials, mild reaction condition and high yield.

General Procedure: A solution of α-haloacetic acid (1 mmol) in 5 mL of anhyd. ethanol was added dropwise to a solution of selenobenzamide (2 mmol) in 25 mL of anhyd. ethanol at room temperature under nitrogen atomosphere, and stirred for 3.5 h (the reaction was monitored by TLC). About 20 mL of water was added to the reaction mixture. The reaction mixture was continued stirred for further 10 min. The mixture was extracted with CH_2Cl_2 (30 mL × 2) and the organic layer was separated, washed with water (20 mL) and dried over sodium sulfate. After removal of solvent, the residue was purified by column chromatography on silica gel (chloroform:ether=10:1 as an eluent) to give bis(carboxyethylmethyl) diselenide **4b** in 90% yield.

Acknowledgments

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References and Notes

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5. Representative data: **4b**: oil[6]; ^{1}H NMR ($CDCl_3$ δppm): 3.85 (q, 2H, J=7.2 Hz, CH_2), 3.54 (s, 2H, CH_2), 1.07 (t, 3H, J=6.9 Hz, CH_3); IR (KBr): 3000, 2960, 1745, 1264, 1100, 1030 cm^{-1}**;** MS (70 eV) *m/z* (%): 334 (M^+, 10.51), 286 (6.34), 254 (4.41), 208 (10.06), 181 (10.72), 153 (9.51), 121 (16.74), 93 (19.51), 59 (55.34), 42 (100); Anal. calcd. for $C_8H_{14}O_4Se_2$: C 28.93, H 4.25; Found C 28.81, H 4.34.
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