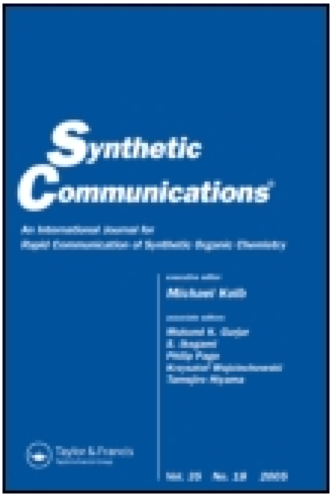

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REACTIONS OF SELENOBENZAMIDE AND ALKYL HALIDES. SYNTHESIS OF DIALKYL SELENIDES AND DISELENIDES

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ABSTRACT: In the absence of base, the reaction of selenobenzamide with alkyl halides gives the dialkyl diselenides as the major product. While the reaction of selenobenzamide and an alkyl halide is carried out in a 1:2 molar ratio and in the presence of strong base, the dialkyl selenides predominate.

Thiocarboamides have been widely used as sulfur transfer reagent, thus symmetrical sulfides are readily synthesized from various alkyl halides and thioacetamide[1-4]. The preparations of sulfur-containing heterocycles from thioacetamide and functionalized halides have also been reported[5]. However, the similar synthesis of dialkyl selenides from alkyl halides and selenoamides has not been reported. In fact the less stable primary selenoamides have only received little attention, although reactions of selenoamides, mainly secondary selenoamides, with the reactive alkyl halides leading to the selenoimidates or the subsequently cyclized Se-containing heterocycles have been known for long time[6-9].

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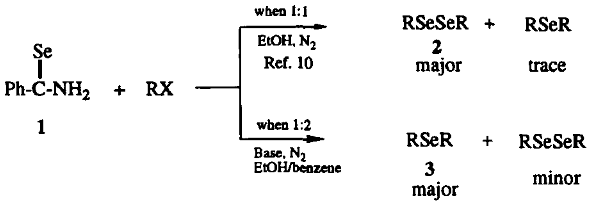
We have recently reported a novel selenium transfer reaction of selenoamides.[10] Alkyl halides react with aromatic primary selenoamides or *N*-phenylselenourea in a 1:1 molar ratio and under the neutral condition to give dialkyl diselenides **2** (Scheme 1). In continuation of our interest in this selenium transfer reaction, we have now found that the reaction of alkyl halides with selenobenzamide in 2:1 molar ratio and in the presence of strong base gives dialkyl selenides as the major product.

When alkyl halides were treated with an equimolar amount of a selenoamide or *N*-phanylselenourea in ethanol at 70 °C under nitrogen, the dialkyl diselenides **2** were obtained in 84 - 91% yield.[10] The formation of diselenides **2** was rationalized by the mechanism shown in Scheme 2. Nucleophilic attack on RX by Se of the selenoamide gave the selenoimidates **4**. The SeR group was then replaced by ethanol from the solvent via addition-elimination to yield intermediates **5** and selenols **6**, which were rapidly converted into dialkyl diselenides **2** on exposure to air during the workup. It was then anticipated that the presence of strong base might enhance the nucleophilicity of selenoimidates and the chance for further reaction with an electrophile. Thus, extra amounts of RX, presence of a base and using less nucleophilic solvent could lead to the further nucleophilic attack of selenoimidates **4** on the second molecule of alkyl halides to give the intermediates **7**. Therefore the reaction of selenobenzamide with two equivalents of an alkyl halide in the presence of base should give dialkyl selenide.

Indeed, when selenobenzamide was treated with 2 equimolar amount of alkyl halides and 2.2 equimolar amount of KOH in ethanol-benzene (1:1 v/v) at 80 °C for 5 hr., dialkyl selenides **3** were given in moderate to good yields (Scheme 1 and Table 1). However, In all these cases, a small amount of dialkyl diselenides was also formed. In this way, a number of dialkyl selenides were prepared, and they were characterized by their ^{1}H NMR and by elemental analyses (Table 1). The by-product, similar to the sulfur transfer reaction of thiocarboamides, is benzonitrile. The selenium transfer reaction described here has provided a general method for preparation of dialkyl selenides. Selenobenzamide can be easily prepared on large scale and is stable on storage.

As an effort at finding the best reaction conditions for the preparation of either dialkyl selenides or diselenides, factors such as bases, solvents and molar ratios of



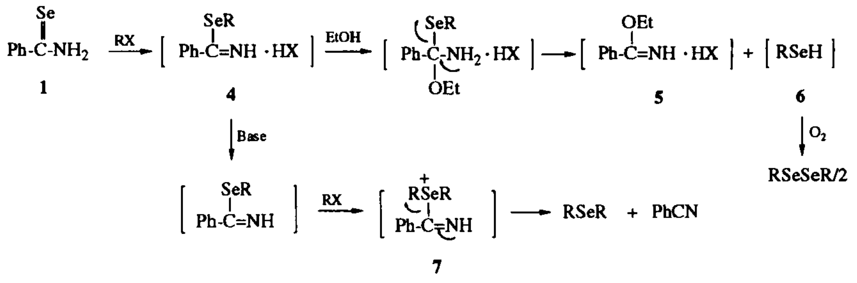
Scheme 1

Table 1. Preparations of dialkyl selenides from selenobenzamide and alkyl halides

RX	RSeR[a]	yield (%)	m.p. (°C)	Lit. m.p. (°C)	^{1}H NMR (δ, $CDCl_3$)
$PhCH_2Cl$	$(PhCH_2)_2Se$[b]	65	44-45	44-45[11]	3.70 (s, 4H), 7.25 (s, 10H)
$n\text{-}C_6H_{13}Br$	$(n\text{-}C_6H_{13})_2Se$	56	oil	oil[12]	0.89 (t, 6H), 1.25-1.75 (m, 16H) 2.55 (t, 4H)
$n\text{-}C_8H_{17}Br$	$(n\text{-}C_8H_{17})_2Se$[c]	50	oil	120/0.1[13]	0.87 (t, 6H), 1.26 (m, 20H), 1.50-1.70 (m, 4H), 2.54 (t, 4H)
$n\text{-}C_{10}H_{21}Br$	$(n\text{-}C_{10}H_{21})_2Se$[d]	44	oil		0.88 (t, 6H), 1.26 (s, 28H) 1.50-1.70 (t, 4H), 2.54 (t, 4H)
$n\text{-}C_{12}H_{25}Br$	$(n\text{-}C_{12}H_{25})_2Se$[e]	42	30-31	25[14]	0.88 (t, 6H), 1.26 (s, 36H) 1.50-1.70 (m, 4H), 2.54 (t, 4H)
$n\text{-}C_{16}H_{33}Br$	$(n\text{-}C_{16}H_{33})_2Se$	39	48-49	51[14]	0.88 (t, 6H), 1.27 (s, 48H), 1.50-1.71 (m, 4H), 2.54 (t, 4H)

a. These were prepared by using KOH as the base. b. Anal. Calcd. for $C_{14}H_{14}Se$: C, 64.37; H, 5.40. Found C, 64.47, H, 5.39. c. Anal. Calcd. for $C_{12}H_{26}Se$: C, 57.83; H, 10.44. Found: C, 57.41; H, 10.77. d. Anal. Calcd. for $C_{16}H_{34}Se$: C, 62.95; H, 11.15. Found: C, 62.70; H, 11.04. e. Anal. Calcd. for $C_{24}H_{50}Se$: C, 69.06, H, 11.99. Found: C, 68.71, H, 12.06.

reactions that influence the product distributions were also examined (Table 2). As mentioned early, the reaction of selenobenzamide and benzyl chloride without base gave predominately the dialkyl diselenides even on a 1:2 molar ratio (runs 1 and 2). The stronger the base, the more selenide is formed if other conditions are the same



Scheme 2

Table 2. Effects of reaction conditions on the products distributions

	$PhCSeNH_2 + PhCH_2Cl \longrightarrow$		$(PhCH_2)_2Se$ +	$(PhCH_2)_2Se_2$
Run	$PhCSeNH_2/PhCH_2Cl$	Reaction conditions		
1	1 : 1	EtOH	1	9
2	1 : 2	EtOH	1	2
3	1 : 2	$Et_3N/EtOH,C_6H_6$	3	1
4	1 : 1	$KOH/EtOH,C_6H_6$	2	1
5	1 : 1.5	$KOH/EtOH,C_6H_6$	2.5	1
6	1 : 2	$KOH/EtOH,C_6H_6$	4	1
7	1 : 2	$EtONa/EtOH,C_6H_6$	10	1
8	1 : 2	$EtONa/C_6H_6$	1	1.5

(runs 3, 6 and 7, EtONa > KOH > Et_3N). At least 2 equimolar amount of benzyl chloride is needed for the synthesis of dialkyl selenide. Benzene alone as the solvent gave the poor result in both yield and selectivity (run 8).Selenobenzamide with 2 equimolar amount of benzyl chloride in ethanol-benzene with sodium ethoxide as the base gave the best results of preparing dialkyl selenides.

EXPERIMENTAL

Melting points were recorded on an electrothermal micro melting point apparatus and are uncorrected. The ^1H NMR spectra were obtained on a FX-90 (90

MHz) spectrometer with TMS as an internal standard. Elemental analyses were performed on a Carlo Erba 1106 elemental analyzer. Selenobenzamide was prepared as previously reported[15]. Anhydrous Ethanol and benzene were used after dried and freshly distilled.

Reaction of benzyl chloride with selenobenzamide

Selenobenzamide (0.40 g, 2 mmol) in ethanol-benzene (1:1 v/v, 20 ml) was added to KOH (0.26 g, 4.6 mmol) in anhydrous ethanol (10 ml) under nitrogen atmosphere. Benzyl chloride (0.51 g, 4 mmol) in anhydrous benzene (10 ml) was then added dropwise at room temperature. After addition, the mixture was refluxed with stirring for 5 hr. On cooling the white inorganic precipitate was filtered off and washed with benzene. The solvent was evaporated under reduced pressure. The yellowish solid was dissolved in CH_2Cl_2 (10 ml), washed with water (3 x 5 ml) and dried over $MgSO_4$. After removal of solvent, the product mixture was analyzed by ^1H NMR and by chromatography to determine the ratio of dibenzyl selenide and dibenzyl diselenide. In most case the mixture was separated by column chromatography (silica gel, cyclohexane) to give pure selenide and diselenide.

The reaction of benzyl chloride and selenobenzamide with triethylamine or EtONa was carried out by the same procedure.

Synthesis of dialkyl selenides, typical procedure

Selenobenzamide (0.40 g) in ethanol-benzene (16 ml) was added to EtONa (4.3 mmol) in ethanol (10 ml). Benzyl chloride (0.51 g) in benzene (10 ml) was added and the mixture was stirred and refluxed for 6 hr. After filtration and removal of the solvent, CH_2Cl_2 (10 ml) was added, washed with water (3 x 5 ml) and dried over $MgSO_4$. The solvent was removed and the resulting solid was purified by recrystallization from petroleum ether to give dibenzyl selenide as yellow crystals (0.34 g, 65%).

Other dialkyl selenides were prepared by the same procedure except for different heating time.

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