Highly chemoselective synthesis of functionalized diselenides from alkyl halides using benzyltriethylammonium tetrathiomolybdate

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A variety of functionalized selenocyanates generated *in situ* from the corresponding alkyl halides undergo a facile reductive coupling on treatment with benzyltriethylammonium tetrathiomolybdate 1 under very mild conditions to give the corresponding diselenides in very good yields.

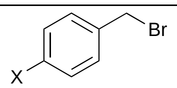
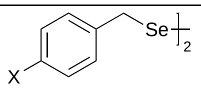
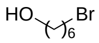
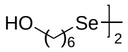
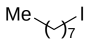
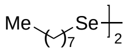
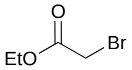
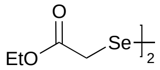
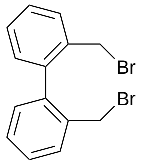
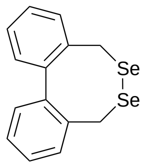
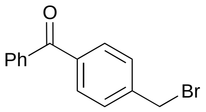
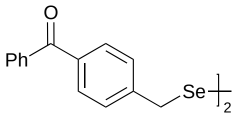
Organoselenium compounds have emerged as important reagents and intermediates in organic synthesis[1] and they also have biological importance as proteins containing selenium are essential components of certain bacterial and mammalian enzyme systems.[2] Hence a convenient synthesis of these selenium compounds in general and functionalised organic diselenides in particular continues to be a challenging task.

From the large number of methods available for the synthesis of diselenides, the most important routes involve either the reaction of metal diselenides on alkyl halides[3] or the preparation of selenols which can be subjected to further oxidation.[4] Recently Salama and Bernad[5] reported that organic selenocyanates, on treatment with $LiEt_3BH$ followed by air oxidation, give the corresponding diselenides in good yields. Most of the methods available are generally useful only for the synthesis of simple diselenides lacking reactive functional groups.

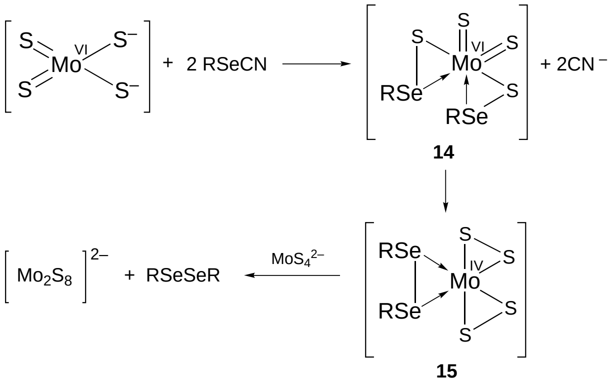
In our earlier work we have demonstrated that benzyltriethylammonium tetrathiomolybdate $[PhCH_2NEt_3]_2MoS_4$ **1** is a useful sulfur transfer reagent in organic synthesis[6] as well as a reagent that can mediate reductive dimerization of alkyl azides[7] and organic thiocyanates.[8] In exploring further the utility of induced internal redox reactions of tetrathiomolybdate **1** in organic synthesis it appeared quite attractive to study the reductive dimerization of organic selenocyanates with **1**. Here we present the results of such an investigation.

Treatment of a number of alkyl halides with KSeCN (1.1 equiv.) in MeCN (25 °C, 0.5 h) generated the corresponding alkyl selenocyanates *in situ* which, on further reaction with tetrathiomolybdate **1** (1.2 equiv., 25 °C, 0.5–24 h), led to the formation of the alkyl diselenides in high yields (85–96%).† The results are summarized in Table 1. As can be seen, except in the case of hydroxy bromide **4** (entry 5), all the substrates reacted with great facility in a short period of time (0.5–6.0 h). Particularly noteworthy are the successful reactions of the substrates **2b**,**c**,**d**, **8** and **12**, which contain easily reducible groups such as nitro, cyano, ester and keto functionalities. The methodology involving use of $LiEt_3BH$[5] or $NaBH_4$[9] for the synthesis of diselenides cannot be applied successfully in many of these cases. This kind of high chemoselectivity obtainable in a room temperature reaction is very unusual. The facile synthesis of a cyclic 8-membered diselenide **11** from dibromide **10** (entry 8) in high yield also demonstrates the high potential of the methodology. Unlike the earlier reported reactions of alkyl selenocyanates, which proceed *via* alkyl selenol intermediates,[5,9] we believe that the present methodology does not involve alkyl selenols as intermediates.‡ A tentative mechanism based on the reactivity of alkyl thiocyanates[8] with tetrathiomolybdate **1** is presented in the Scheme 1. It is likely that, in the reaction of organic selenocyanates, the attack of MoS_4^{2-} on the selenium of selenocyanate leads to mononuclear molybdenum species of type **14**. The second stage of the reaction can be represented as an induced internal electron-transfer from a sulfur ligand to Mo^{VI} to produce Mo^{IV} species **15**.[10] Further reaction of **15** with **1** results in the formation of alkyl diselenides and $Mo_2S_8^{2-}$.§

Table 1 Formation of diselenides

Entry	Starting material	*t*/h[a]	Product	Yield (%)[b,c]
				
1	**2a** X = H	0.5	**3a**	89
2	**2b** X = NO_2	2	**3b**	90
3	**2c** X = CN	1	**3c**	86
4	**2d** X = CO_2Et	6	**3d**	95
5	 **4**	24	 **5**	96
6	 **6**	0.5	 **7**	85
7	 **8**	0.5	 **9**	90
8	 **10**	0.5	 **11**	88
9	 **12**	4	 **13**	87

[a] Time refers to conversion of selenocyanate to diselenide. [b] Refers to isolated yield. [c] All the products exhibited expected analytical and spectral data.



Scheme 1

In conclusion, we have demonstrated that a variety of functionalized alkyl diselenides can be synthesised in high yield from alkyl halides *via* alkyl selenocyanates under mild conditions. Further work is in progress to extend this methodology to unsymmetrical diselenides and seleno sulfides.

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Footnotes

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† No trace of selenol could be detected in the reaction mixture, and tetrathiomolybdate **1** does not convert selenols to diselenides.

‡ *Typical procedure*. To a solution of benzyl bromide **2a** (1 mmol) in MeCN (5 ml) was added KSeCN (1.1 mmol). The mixture was stirred at room temperature (25 °C) for 0.5 h (until the starting material had disappeared, as shown by TLC), and benzyltriethylammonium tetrathiomolybdate **1** (1.2 mmol) was added. The mixture stirred for 0.5 h, the solvent was evaporated *in vacuo* and the black residue thus formed was extracted with CH_2Cl_2–Et_2O (1 : 9, 20 ml × 5) and filtered through a Celite pad. The filtrate was concentrated and the crude product was purified by column chromatography (silica gel, light petroleum (60–80 °C)–ethyl acetate, 9 : 1) to yield dibenzyl diselenide **3a** as a solid, mp 90–91 °C (lit.,[3] 90–91 °C) in 87% yield.

§ The IR spectrum (KBr) of the molybdenum byproduct shows a strong absorption at 515 cm^{-1} assignable to a persulfido molybdenum species.

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