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ONE-POT TWO-STEP APPROACH TO SELENIDES. PHASE-TRANSFER CATALYZED SYNTHESIS OF ω-HYDROXYALKYL SELENIDES

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ABSTRACT: ω-hydroxyalkyl selenides were synthesized in good yields under phase-transfer conditions which involved hadrazine reduction on selenium powder and then alkylation with ω-haloalkyl alcohols in the presence of TBAB, reduction the resulting diselenides with KBH_4 followed by treatment with alkyl halides.

ω-Hydroxyalkyl selenide compounds are valuable intermediates and find wide applications both in chemistry[1-2] and biochemistry.[3] For example, have been utilized for the synthesis of a variety of functionalized molecules,[1-2, 4] such as allyl alcohols, epoxides, olefins, α,β-unsaturated carbonyl compounds and other compounds. They also have been used to prepare organoselenium alkylating

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agents, analogues of nitrogen and sulfur mustards, which show strong biological activities such as antineoplastics and cytotoxity.[3] Our interests in this kind of compounds stemmed from that they can be incorporated through their hydroxy groups into polymer supports and outside edges of macrocyclic compounds, thus lead to polymer selenium ligands and exocyclic selenium ligands. These type ligands have shown high binding affinity toward heavy metal and transition metal cations[5] and their transition metal complexes exhibited attractive catalytic properties,[6, 7] thus may be used such as in catalysis and separation science. In addition, ω-hydroxyalkyl selenides with two ω-hydroxyalkyl groups are main unites of selenacrown ethers, a novel type of crown ethers.[8]

Several methods have been reported for the synthesis of ω-hydroxyalkyl selenides,[2] including (A) opening of epoxides with selenide anions (RSe^-); (B) treatment of epoxides or carbonyl compounds with selenium-stabilized carbanions ($PhSeC^-R_2$) or selenoxide-stabilized carbanions ($PhSe(O)C^-R_2$) which are generated by lithation of selenoketals with n-BuLi or by deprotonation of selenoxide by LDA, respectively; (C) reaction of α-keto-selenides with $LiAlH_4$ or $NaBH_4$ or Grignard reagents; (D) addition of organoseleneyl halides to olefins;[9] (E) reduction of ω-hydroxyalkyl selenocyanates, which are prepared from ω-haloalkyl alcohols and KSeCN, with $NaBH_4$ in dry ethanol followed by addition of alkyl halides;[10] (F) reduction of bis(ω-hydroxyalkyl)diselenides by metal borohydride in aprotic solvent and then by treatment with alkyl halides.[6]

Although these methods have their own merits, they suffer from more or less disadvantages, such as uneasily accessible precursors (e.g., selenoketals, selenoxides), stern conditions (low temperature, dry conditions), highly toxic reagents (e.g. KSeCN) and tedious work-up.

With above considerations, we set out to find more general and convenient methods for the preparation of ω-hydroxyalkyl selenides. Very recently, we have designed a facile way to dialkyl diselenides, which involved phase-transfer catalyzed nucleophilic substitution of alkyl halides with diselenide anion (Se^{2-}).[11] Since the yields and purity are high, it occurred to us that the resulting diselenides (RSeSeR) may be directly reduced without purification to alkyl selenide anion (RSe^{-}), and then alkylated by another alkylating reagents under the same phase-transfer conditions to bestow selenides in the same pot.[12] This notion has been experimentally demonstrated and here we present the results.

The synthetic route is shown in Scheme 1. Selenium powder was reduced to diselenide anion (Se^{2-}) with hydrazine in water and then reacted with ω-hydroxyalkyl halides in the presence of TBAB (tetrabutylamonium bromide) to afford the corresponding bis(ω-hydroxyalkyl)diselenides, which were further reduced by potassium borohydride followed by alkylation with alkyl halides to offer the desired ω-hydroxyalkyl selenides. Their structures were identified by ^{1}HNMR and MS, which were in accordance with that in literatures.[6, 10] The results are summarized in Table 1.

Scheme1

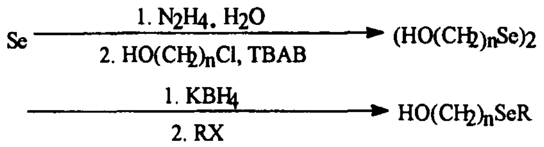

Table 1 Synthesis of ω-hydroxyalkyl selenides by one-pot two-step procedure

entry	n	R	Yield[a] (%)
1	2	$HO(CH_2)_2Cl$	76
2	2	C_2H_5I	73
3	2	$CH_2=CHCH_2Cl$	61
4	2	$C_6H_5CH_2Cl$	64
5	3	$HO(CH_2)_3Cl$	81
6	3	C_2H_5I	68
7	3	$C_6H_5CH_2Cl$	71

[a] The yields are based on the amount of selenium powder.

The present one-pot two-step procedure[13] possessed several features: Firstly, it is very convenient. The reactions were performed under easy-to-meet conditions (in contrast to low temperature and dry solvents[2, 10]) and the work-up is very simple (in contrast to two-flask preparation and troublesome work caused by the use of aprotic solvents); Secondly, ω-hydroxyalkyl selenides can be obtained in good yields (61-81%), which are comparable or even higher than those reported before. For example, the yield for ethyl 2-hydroethyl selenide is

73% in our method, whereas it is 62% (total yield of two-step reaction) in method D.[10] Finally, the starting materials are very easily obtainable. Note that though compound bis(2-hydroxyethyl)selenide (entry 3) and bis(3-hydroxypropyl)selenide (entry 6) can also be obtained via reduction of selenium powder to selenide anion (Se^{2-}) with metal borohydride followed by alkylation with 2-chloroethanol and 3-chloropropanol, respectively, and the yields are comparable, much less amount of expensive metal borohydride[14] is needed in our new method. Another point is that though the present method has only been applied to the synthesis of ω-hydroxyalkyl selenides, it should also be applicable to the synthesis of other selenides. [12]

In a word, we have described a very convenient and efficient method for the preparation of ω-hydroxyalkyl selenides. Their uses in catalysis and separation science will be reported in due course.

References and Notes

1. Liotta, D. *Acc. Chem. Res.*, **1984**, 17, 28.
2. Clive, D.L.J. *Tetrahydrons*, **1978**, 34, 1049, and references therein.
3. Kang, S.I. and Spears, C.P. *J. Pharm. Sci.*, **1990**, 79, 2587, and references therein.
4. Krief, A. *Tetrahydrons*, **1980**, 36, 2531; Laboureur, J.; L. Domont, W. and Krief, A., *Tetra. Lett.*, 1984, 25, 4569; Toshimitsu, A.; Hayashi, G.; Kerav, K. and Vemura, S. *J. Chem. Soc. Perkin Trans. 1*, **1986**, 343.

5. Hope, E.G. and Levason, W. *Coord. Chem. Rev.*, **1993**, 122, 161.

6. Chen, Z. MS Thesis, Wuhan University, **1993**.

7. We recently found that calix[4]arene selenoether platinum complex possessed unusual regioselectivity in styrene hydrosilylation.

8. For review on selenacrowns, Li, W.P.; Liu, X.F. and Xu H.S. *Huaxue Tongbao.*, **1995**, 7,7.

9. Toshimitsu, T.; Aoai, T.; Owadam, H.; Vamura, S. and Okano, M. *Tetrahydrons*, **1985**, 41, 5301.

10. Kang, S.I. and Spears, C.P. *Synthesis*, **1988**, 133.

11. Hu, X.B.; Tian, Z.J.; Lu, X.R. and Chen, Y.Y. *Synth., Commun.*, **1997**, 27, 553.

12. Syper and Mlochoveski ever reported a phase-transfer method for the synthesis of methyl and phenyl selenides. Nevertheless, the method was not applicable to the synthesis of other selenides, and purified diselenides were used. Syper, L. and Mlochoveski, J. *Synthesis*, **1984**, 439.

13. A general procedure for the preparation of ω-hydroxyalkyl selenides: To the mixture of selenium (4.0g, 50mmol) and sodium hydroxide (2.0g, 100mmol) in water (30ml), 85% hydrazine hydrate (1.0ml, 17mmol) was added dropwise under nitrogen. Stirring and heating it for about 3hr until all the selenium was consumed. Then 0.3g TBAB and ω-haloalkyl alcohol (50mmol) in ethyl ether (20ml) were added and refluxed. When the aqueous layer was nearly clear KBH_4 (90mmol) and NaOH (60mmol) was added and refluxed until the solution became colorless,

followed by dropping a solution of alkyl halide (75mmol) in ether (20ml). After refluxing 8hr, the mixture was allowed to cool down to room temperature. The ether layer was separated and the aqueous layer was extracted with ether for several times. The organic layers were combined and washed with water followed by brine and dried over anhydrous magnesium sulfate. After removing the solvent off the residue was purified by column chromatography on silica gel to afford pure product.

14. Rongalite can also be used in the preparation and it is cheaper, but it easily deteriorates.

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