A Novel Synthetic Approach to β-Arylselenenyl Tertiary Alcohols by the One-Pot Reaction of Chloromethyl Selenides and Ketones Promoted by Samarium Diiodide

Xian Huang* and De-Hui Duan

Department of Chemistry, Hangzhou University, Hangzhou Zhejiang 310028, P.R.China

Fax: 86 571 8807077; E-mail: huangx@public.hz.zj.cn

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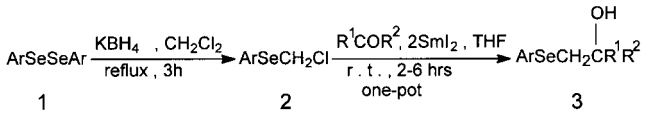
Abstract: At ambient temperature, β-arylselenenyl tertiary alcohols can be conveniently synthesized with samarium diiodide, chloromethyl selenides and ketones by one-pot method in high yields.

β-Hydroxyalkyl selenides are valuable intermediates for the synthesis of various selenium-free compounds[1]. They have been reduced to alcohols, transformed to alkenes, rearranged to ketones and used as the precursors of epoxides and allyl alcohols. β-Hydroxyalkyl selenides have been already synthesized by the reaction of α-selenoalkyllithiums towards aldehydes or ketones[2]. Another method was by the addition reaction of phenylselenenyl chloride to olefins followed by hydrolysis[3]. Although the former is the most general method, the necessary selenoacetals can not be easily obtained[4], and the preparations and reactions of α-selenoalkyllithiums are required at low temperature (usually at -78°C), which causes some inconvenient operation. With regard to the latter, for the absence of regioselectivity in the addition reaction, two mixtures are usually obtained, which limited its use. Now we provide a novel approach to β-arylselenenyl tertiary alcohols, one important type of β-hydroxyalkyl selenides. Target products are obtained by a one-pot procedure with chloromethyl arylselenides, ketones and samarium diiodide under very mild conditions. With a modified literature[5] method, chloromethyl arylselenides can be also conveniently prepared[6] (see **Scheme 1**).

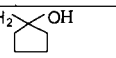
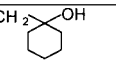
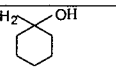


Ar = Ph , p- MeC$_6$H$_4$
R^1, R^2= Me , Et , n-Pr , n-Bu , -(CH$_2$)$_4$ - , -(CH$_2$)$_5$ -

Scheme 1

Recently, applications of samarium diiodide in organic synthesis have become popular[7]. Kagan firstly found that as well as being a powerful reducing agent, SmI_2-THF solution could promote efficiently alkylations of ketones by alkyl halides[8]. Alkyl iodide, bromide and sulfonates have achieved satisfactory results. When alkyl chlorides (even allyl chlorides) were used, long reaction time and low yields were encountered. However, in our experiments, chloromethyl selenides can act as an excellent arylselenomethylation agent. At room temperature, the alkylation reactions are completed over 2-6 hrs in high yields (usually over 70%). Therefore, the ability of the selenium functional group to stabilize adjacent carbanions must facilitate greatly the alkylation reaction. Except for acetophenone, the reaction towards alkyl ketones and cycloalkylketones can achieve good results by the simultaneous addition of ketones and chloromethyl selenides to the samarium diiodide solution of THF. Low yield (30%) of tertiary alcohol is obtained in the reaction of acetophenone by the above procedure. If chloromethyl selenide is added prior to the addition dropwise of the acetophenone solution, the yield can be improved to 60%. The alkylation of aldehydes is unsuccessful because the direct reduction to alcohols and/or pinacol coupling dominates the reaction. Attempt of a Grignard procedure fails, too. Even in the absence of a proton donor, chloromethyl selenides are reduced to methyl aryl selenides. The representative experimental results[9] are summarized in **Table 1**.

Table 1

Entry	ArSeCH$_2$Cl	Ketones	Products$^\alpha$	time (h)	Yield (%)$^\beta$
1	PhSeCH$_2$Cl 2a	acetone	PhSeCH$_2$C(OH)(CH$_3$)$_2$ 3a	2	75
2	2a	2-butanone	PhSeCH$_2$C(OH)(CH$_3$)C$_2$H$_5$ 3b	4	83
3	2a	2-pentanone	PhSeCH$_2$C(OH)(CH$_3$)Pr-n 3c	4	78
4	2a	cyclopentanone	 3d	3	70
5	2a	cyclohexanone	 3e	4.5	78
6	p-TolylSeCH$_2$Cl 2b	2-butanone	p-TolylSeCH$_2$C(OH)(CH$_3$)C$_2$H$_5$ 3f	3.5	75
7	2b	2-pentanone	p-TolylSeCH$_2$C(OH)(CH$_3$)Pr-n 3g	5.5	85
8	2b	cyclohexanone	 3h	4	72
9	2b	acetophenone	PhSeCH$_2$C(OH)(CH$_3$)Ph 3i	2.5	60$^\gamma$

α all products are oil compounds at room temperature.

β yields of pure compounds. Satisfactory spectra data (IR, ^{1}H-NMR and mass spectra) and elemental analyses were obtained for all new compounds.

γ slowly adding the acetophenone solution to the mixture solution of SmI_2 and chloromethyl phenyl selenide over 2 hrs, and continuing to stir for 30 mins.

In conclusion, we found a novel method for one-pot preparation of β-hydroxyalkyl selenides. Mild reaction conditions, convenient operation, available materials and high yields make it attractive.

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References and Notes

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6 The following procedure is typical for the preparation of chloromethyl arylselenides. A 500ml three-necked flask equipped with a magnetic bar, a reflux condenser, a nitrogen inlet and a 100ml pressure equalizing addition funnel, was charged with dry dichloromethane (300ml) and potassium borohydride (4.86g, 90mmol). A diphenyl diselenide (9.4g, 30mmol) suspending solution of ethanol (75ml) was poured into the funnel. The reaction flask was stirred and gently refluxed while the suspending solution was added in batches over two hours. When the solution lost its yellow colour, stirring was continued for 30mins. The crude mixture was washed with dilute HCl, water, and brine, then it was dried with $MgSO_4$ and the solvent was evaporated. Distillation of the residue provided chloromethyl phenyl selenide (10.3g, 50mmol, 83%) **2a** as an almost colourless oil. 90-92/3mmHg.(Lit.[10] 63-65/0.1torr). ^{1}H NMR δ_H (ppm): 4.92 (s, 2H), 7.20-7.65 (m., 5H).

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9 Typical procedure. A SmI_2 (2.0mmol) solution of THF(20ml)was placed in a 50ml two-necked flask, 1mmol of 2-butanone in 5ml of THF was added, then 1mmol of chloromethyl phenylselenide in 5ml of THF was introduced. Reaction was performed under nitrogen at room temperature. After 4hrs, the initial blue solution of SmI_2 turned yellow, indicating the end of the reaction. The mixture was worked up with the dilute HCl(0.1N). Organic product was extracted twice with ether. The organic layer was washed with water, sodium thiosulfate, water and brine. After the solution was dried over $MgSO_4$, solvent was removed. The product was separated from the residue through preparative TLC (silica gel)with cyclohexane /ethyl ether (4:1) as eluent to give 2-methyl-1-phenylselenobutan-2-ol **3b** (Oil,83%). IR ν_{max}/cm^{-1}: 3500; 2980; 2940; 1590; 1480; 1440; 1380; 730; 680. ^{1}H NMR(CCl_4/TMS) δ_H (ppm): 0.89 (t, 3H, J=7.1Hz), 1.17 (s, 3H), 1.43 (q, 2H, J=7.1Hz), 1.83 (br s, 1H), 3.02 (s, 2H), 7.10-7.60 (m, 5H). MS (*m/z*, relative intensivity %) (EI): 244(^{80}Se,100) and 242(^{78}Se,49) (M^+), 227(35), 172(82), 157(20), 73 (46). Anal. calcd. for $C_{11}H_{16}OSe$ C%,54.32; H%,6.63. Found: C%,54.15;H%, 7.01.

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