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# Cesium hydroxide-catalyzed hydrothiolation of alkynyl selenides to highly stereo- and regioselectively synthesize (*Z*)-1-organoseleno-2-arylthio-1-alkenes

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## Abstract

In the presence of catalytic amount of cesium hydroxide the hydrothiolation of alkynyl selenides occurred at room temperature in DMF under nitrogen atmosphere to give exclusive (*Z*)-1-organoseleno-2-arylthio-1-alkene in excellent yields. It could provide a new and expedient way for the preparation of (*Z*)-1-arylseleno-2-arylthio-1-alkene.

*Keywords:* Hydrothiolation; Cesium hydroxide; Alkynyl selenides; (*Z*)-1-Organoseleno-2-arylthio-1-alkene

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The synthesis and application of chalcogenide alkenes has attracted chemist attention because of their chemo-, region-, and stereoselective reactions. The chalcogenide atom (S, Se) exercises a stabilizing effect on neighboring positive as well as negative charges. This makes the double bond in chalcogenide alkenes responsive toward both nucleophilic and electrophilic attack, an extremely useful feature for organic synthetic purpose [1,2]. Among the common chalcogenide alkenes, 1,2-dichalcogenide alkenes are of much importance because of their use as bidentate ligands in coordination chemistry, precursors of new optical materials for microelectronics, and important intermediates for organic synthesis [1]. The unsymmetrical 1,2-dichalcogenide alkenes, which bond to two different organochalcogen groups in the double bond, seem more significant than the corresponding symmetrical 1,2-dichalcogenide alkenes, the reason is that the different organochalcogen groups such as organothio and organoseleno group present different natural reactivities. Many procedures have been developed to prepare symmetrical 1,2-dichalcogenide alkenes, for example, the transition-metal [3–12] or cesium hydroxide-catalyzed [13–15] S–S and Se–Se bond addition to alkynes. Thiols or selenols addition to terminal alkynyls could introduce organothio or organoseleno group in the double bond, it only suited for the preparation of mono-chalcogenide substituted alkenes, with activated alkynes such as acetylenic esters and ketones, the addition has been performed under basic conditions, using reagents such as KOH [16] and triethylamine [17], however, for unactivated alkynes, the use of radical initiators [18], transition-metal catalysts [19,20], and high temperatures [21] has been required. But at high temperature or use of

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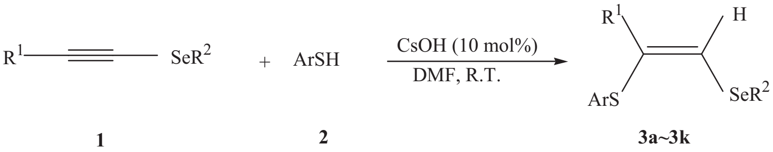


Scheme 1. The hydrothiolation of alkynyl selenides catalyzed by cesium hydroxide.

radical initiators, the addition reactions often resulted in the formation of both *Z*- and *E*-isomers, the separation of the *Z*- and *E*-isomers was often quite difficult. To our knowledge, there were few reports concerning the synthesis of unsymmetrical 1,2-dichalcogenide alkenes [22]. Although the addition of unsymmetrical diorganoyl dichalcogenides ($R^2S\text{-}SeR^1$) to terminal alkynes afforded (*Z*)-1-arylseleno-2-arylthio-1-alkenes with highly stereoselective [23], the procedure needed use of water-sensitive butyl lithium, moreover it only suited for this substratum containing hydroxyl group on the 3-position of alkynese, such as propargylic alcohols. Our group investigated the above addition catalyzed by cesium hydroxide, and found that the $R^2S\text{-}SeR^1$ reacted with terminal alkynes in the presence of 10 mol% cesium hydroxide at room temperature in commercial THF to give exclusive (*Z*)-1-arylseleno-2-arylthio-1-alkenes with excellent yields [24]. But the reagent ($R^2S\text{-}SeR^1$) is not easily obtained. Alkynyl selenides and sulfides are important intermediates and are readily prepared, their hydrothiolation and hydroselenation could form unsymmetrical 1,2-dichalcogenide alkenes. In this paper, we report that cesium hydroxide catalyze addition of thiols to alkynyl selenides to synthesize (*Z*)-1-organoseleno-2-arylthio-1-alkenes.

The experiments showed that the addition of thiols to alkynyl selenides could efficiently occur in the presence of 10 mol% cesium hydroxide at room temperature in commercial DMF under nitrogen atmosphere to give exclusive (*Z*)-1-organoseleno-2-arylthio-1-alkenes with excellent yields (Scheme 1). The results are summarized in Table 1.

Inspection of Table 1 shows that the reaction worked well for a variety of thiols and alkynyl selenides. The results also indicated that the reaction is not sensitive to the electronic nature of the functional groups present in the thiols and organoselenium groups. Either electron donating or electron withdrawing groups were applied leading to corresponding (*Z*)-1-organoseleno-2-arylthio-1-alkenes in high yields. The method not only suits for 3-hydroxylpropynyl selenides but also suits for alkoxy or aryloxy propynyl selenides and phenylselenide, but it also has some limitation, for example, almost no reaction was observed with alkynes bearing an alkyl group directed at the triple bond, in this case we observed only traces of product.

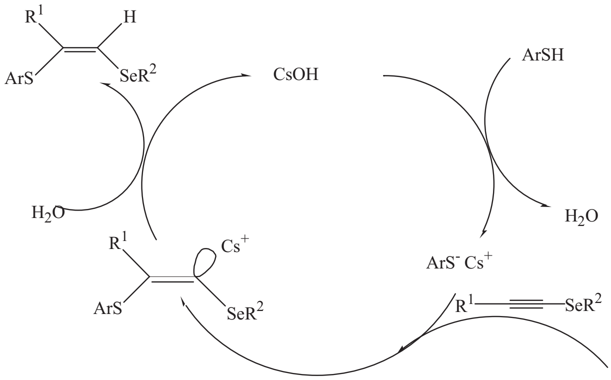
Table 1
The synthesis of (*Z*)-1-arylseleno-2-arylthio-1-alkenes.

| Compd. | $R^1$ | $R^2$ | ArSH | Time (h) | Yields (%) |
|---|---|---|---|---|---|
| **3a** | $CH_3OCH_2$ | Ph | *p*-$CH_3C_6H_4SH$ | 3.0 | 98 |
| **3b** | $CH_3OCH_2$ | Ph | $C_6H_5SH$ | 3.0 | 95 |
| **3c** | $CH_3OCH_2$ | Ph | *p*-$ClC_6H_4SH$ | 3.0 | 97 |
| **3d** | $CH_3OCH_2$ | *p*-$CH_3C_6H_4$ | $C_6H_5SH$ | 3.5 | 96 |
| **3e** | $CH_3OCH_2$ | *p*-$ClC_6H_4$ | $C_6H_5SH$ | 4.0 | 93 |
| **3f** | $CH_3OCH_2$ | $CH_3$ | $C_6H_5SH$ | 4.0 | 90 |
| **3g** | $CH_3OCH_2$ | $CH_3CH_2$ | $C_6H_5SH$ | 4.5 | 86 |
| **3h** | $HOCH_2$ | Ph | *p*-$CH_3C_6H_4SH$ | 3.0 | 95 |
| **3i** | $HO(CH_3)_2C$ | Ph | $C_6H_5SH$ | 5.0 | 86 |
| **3j** | $PhOCH_2$ | Ph | $C_6H_5SH$ | 3.0 | 95 |
| **3k** | Ph | Ph | $C_6H_5SH$ | 2.0 | 92 |

Table 2
The yields of the addition of phenyl thiol to 3-methoxy propynyl phenylselenide using various alkali metal hydroxides as catalyst.

| Catalyst | LiOH | NaOH | KOH | RbOH | CsOH | $Cs_2CO_3$ |
|---|---|---|---|---|---|---|
| Yield[a] (%) | 13 | 45 | 57 | 68 | 98 | 59 |

[a] Isolated yield.



Scheme 2. The mechanism for the addition of thiol to alkynyl selenide.

We also compared the catalytic activity of other alkali metal hydroxides; the results are shown in Table 2. As is apparent from Table 2, the cesium hydroxide showed the strongest catalytic activity for the reaction. The other alkali metal hydroxides showed lower catalytic activity. The difference in the catalytic activity among the hydroxides is ascribed to the differing sizes of the alkali metal ions [25]. The cesium ion, which has the largest ionic radius, is anticipated to be only weakly paired with the counter-anion. Thus the *in situ* generated cesium aryl sulfide (ArSCs) is considered to be more nucleophilic than the sulfide conjugated with other alkali metals.

A possible reaction mechanism for the addition reaction of thiols to alkynyl selenide is depicted in Scheme 2. First, arylthiols reacted with cesium hydroxide to give cesium arylsulfides and $H_2O$. Second, the cesium arylsulfides underwent nucleophilic addition to the alkynyl selenides to form (*Z*)-1-organoseleno-2-arylthiovinylic anion, which reacted with water to give product (*Z*)-1-organoseleno-2-arylthio-1-alkenes and catalyst cesium hydroxide.

The analysis of $^1$H NMR and $^{13}$C NMR spectra showed that all (*Z*)-1-organoseleno-2-arylthio-1-alkenes prepared presented data in full agreement with their assigned structures. The stereochemistry of trisubstituted alkenes was determined by NOESY experiments. The NOESY NMR experiment of compound **3a** showed only a correlation between the vinylic hydrogen and the methylene hydrogen bonded to the methoxy, indicating a *cis* relation between them.

In conclusion, a mild, efficient and highly stereo-, and regioselective method for the synthesis of (*Z*)-1-organoseleno-2-arylthio-1-alkenes was developed. The present method use air-stable cesium hydroxide as catalyst, require neither the high temperature nor the use of expensive transition metals. It could provide a new and expedient way for the preparation of (*Z*)-1-organoseleno-2-arylthio-1-alkenes. The hydroselenolation, hydrophosphination of alkynyl sulfides and selenides as well as phosphines catalyzed by cesium hydroxide will be reported soon.

## 1. Experimental

Arylthiol (1.2 mmol) and cesium hydroxide (0.1 mmol) were added to a solution of alkynyl selenide (1.0 mmol) in DMF (2.0 mL). The reaction mixture was stirred at room temperature under a nitrogen atmosphere for a period time listed in Table 1. Then 20 mL of water was added to the mixture and extracted with petroleum ether (3 × 30 mL). The combined organic phase was dried over anhydrous $Na_2SO_4$, and concentrated under vacuum. The residue was purified by flash chromatography on silica gel giving products. Compound **3a**: $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 2.26 (s, 3H), 3.02 (s, 3H), 3.81 (s, 2H), 7.04 (d, 2H, $J = 8.0$ Hz), 7.08 (s, 1H), 7.23–7.25 (m, 5H), 7.50–7.52 (m, 2H). $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 21.1, 57.9, 74.7, 127.7, 129.3, 129.4, 129.8, 130.5, 130.7, 131.8, 131.8, 133.0, 137.2. MS(EI), *m/z* (%): 350 ($M^+$, 100). Anal. Calcd. for $C_{17}H_{18}OSSe$: C 58.38, H 5.16, Found: C 58.45, H 5.13.

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## References

[1] I. Beletskaya, C. Moberg, Chem. Rev. 99 (1999) 3435.
[2] T. Kondo, T. Mitsudo, Chem. Rev. 100 (2000) 3205.
[3] H. Kuniyasu, A. Ogawa, S.I. Miyazaki, et al. J. Am. Chem. Soc. 113 (1991) 9796.
[4] C.C. Schneider, B. Godoi, M. Prigol, C.W. Nogueira, et al. Organometallics 26 (2007) 4252.
[5] A.V. Moro, C.W. Nogueira, N.B.V. Barbosa, J. Org. Chem. 70 (2005) 5257.
[6] V.P. Ananikov, M.A. Kabeshov, I.P. Beletskaya, J. Organomet. Chem. 687 (2003) 451.
[7] V.P. Ananikov, M.A. Kabeshov, I.P. Beletskaya, Synlett 6 (2005) 1015.
[8] V.P. Ananikov, I.P. Beletskaya, Org. Biomol. Chem. 2 (2004) 284.
[9] S.I. Usugi, H. Yorimitsu, H. Shinokubo, et al. Org. Lett. 6 (2004) 601.
[10] M.J. Dabdoub, P.J. Guerrero Jr., Tetrahedron Lett. 42 (2001) 7167.
[11] S.I. Watanabe, E. Mori, H. Nagai, et al. J. Org. Chem. 65 (2000) 8893.
[12] X. Huang, X.H. Xu, W.X. Zheng, Synth. Commun. 29 (1999) 2399.
[13] J.C. Zeng, R.L. Lu, X.H. Xu, Chin. J. Org. Chem. 24 (2004) 1482.
[14] K.B. Zou, R.H. Qiu, D.W. Fang, et al. Synth. Commun. 38 (2008) 2237.
[15] K.B. Zou, X.H. Yin, W.Q. Liu, et al. Synth. Commun. 39 (2009) 2646.
[16] D.H. Wadsworth, M.R. Detty, J. Org. Chem. 45 (1980) 4611.
[17] E.I. Heiba, R.M. Dessau, J. Org. Chem. 32 (1967) 3837.
[18] A. Ogawa, T. Ikeda, K. Kimura, et al. J. Am. Chem. Soc. 121 (1999) 5108.
[19] A. Kondoh, H. Yorimitsu, K. Oshima, Org. Lett. 9 (2007) 1383.
[20] F. Manarin, J.A. Roehrs, M. Prigol, et al. Tetrahedron Lett. 48 (2007) 4805.
[21] L. Benati, P.C. Montevecchi, P. Spagnolo, J. Chem. Soc., Perkin Trans. 1 (9) (1991) 2103.
[22] A.L. Braga, E.F. Alves, C.C. Silveira, et al. Tetrahedron Lett. 41 (2000) 161.
[23] V.P. Ananikov, M.A. Kabeshov, I.P. Beletskaya, Organometallics 24 (2005) 1275.
[24] This work will be reported in another paper.
[25] R.L. Lu, X.H. Xu, W.Q. Liu, et al. Chin. Chem. Lett. 16 (2005) 325.