A novel preparation of chiral (*Z*)-*O*-alkyl enol ethers from alkenylselenonium salts

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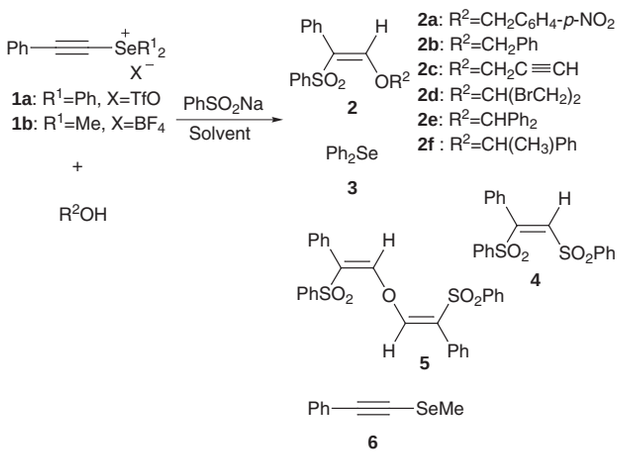
Received (in Cambridge) 30th June 1999, Accepted 30th June 1999

The reactions of alkenylselenonium salts with chiral secondary alkoxides afforded chiral (*Z*)-*O*-alkyl enol ethers in good yields and, especially in the case of sterically hindered secondary cyclic alcohols, the best results were obtained from reactions of dimethylalkenylselenonium salt 7b with alkoxides prepared from PhLi and the corresponding alcohols in THF at −78 °C.

Chiral (nonracemic) *O*-alkyl enol ethers are widely used in various asymmetric reactions such as Diels–Alder reactions,[1] ketene [2+2] cycloadditions,[2] Bradsher cycloadditions,[3] 1,3-dipolar cycloadditions,[4] and tandem [4+2]/[3+2] cycloadditions.[5] Furthermore these materials are enantiomerically pure chiral auxiliaries for the total synthesis of natural products.[6] On the other hand, an α-vinylic hydrogen atom of an enol ether can be substituted with *t*-BuLi to form a vinyllithium, which reacts with an aldehyde or a ketone to produce an allyl alcohol.[7] The application of chiral *O*-alkyl enol ethers to this reaction could lead to a new type of asymmetric synthesis of chiral allyl alcohols. There have been several reports on the preparation of chiral *O*-alkyl enol ethers.[8] Only two methods are frequently utilized; namely mercuric salt-catalyzed vinyl group exchange between an alcohol and an alkyl vinyl ether,[9] and stereoselective reduction of an acetylenic ether, which is prepared from an alcohol and a trichloroethylene, by Lindlar hydrogenation or Birch-type reduction.[10] However, these methods have low chemical yields and stereoselectivity.

We previously reported the reactions of diphenyl(phenylethynyl)selenonium triflate with various nucleophiles.[11] The selenonium salt reacted with sodium benzenesulfinate in various alcohols to give exclusively (*Z*)-β-alkoxy-α-phenylsulfonylstyrenes.[11a] The present paper describes a convenient stereoselective one-step synthesis of chiral (*Z*)-*O*-alkyl enol ethers bearing a β-hydrogen on the styrene moiety.

The reactions of alkynylselenonium salts **1** with a range of alcohols and 1.1 equiv. of sodium benzenesulfinate in aprotic solvents at room temperature were investigated (Scheme 1) and



Scheme 1

the results are summarized in Table 1. The reactions of diphenylalkynylselenonium salt **1a** with *p*-nitrobenzyl alcohol and sodium benzenesulfinate in THF or DMSO for 3 h gave complex mixtures (entries 1 and 2), whereas the reaction in MeCN proceeded within 30 minutes to give β-sulfonyl enol ether **2a** in 91% yield (entry 3). The reactions with other primary alcohols also afforded *O*-alkyl enol ethers **2b**, **c** in high yields in a short reaction time (entries 4 and 5). In the case of secondary alcohols, however, their bulkiness affected the yields of the enol ethers and in particular, the reaction with the sterically hindered secondary cyclic alcohol (−)-menthol did not produce an enol ether (entry 13). Increasing the amount of alcohol did not improve the yield (entries 9 and 10). When the yield of *O*-alkyl enol ether was low, by-products, 1,2-bis(phenylsulfonyl)alkene **4** and divinyl ether derivative **5** were obtained. The reactions of dimethylalkynylselenonium salt **1b**, which was less bulky than **1a**, gave good results, especially at low temperatures (entries

Table 1 The reactions of alkynylselenonium salts and various alcohols with 1.1 equiv. of $PhSO_2Na$

Entry	1	ROH (equiv.)	Solvent	Temp./°C	Time/h	Products (% yield)[a]
1	**1a**	*p*-$NO_2C_6H_4CH_2OH$ (1.5)	THF	rt	3.0	Complex mixture
2	**1a**	*p*-$NO_2C_6H_4CH_2OH$ (1.5)	DMSO	rt	3.0	Complex mixture
3	**1a**	*p*-$NO_2C_6H_4CH_2OH$ (1.0)	MeCN	rt	0.5	**2a** (91) **3** (93)
4	**1a**	$PhCH_2OH$ (1.5)	MeCN	rt	0.5	**2b** (90) **3** (95)
5	**1a**	$HC{\equiv}CCH_2OH$ (1.5)	MeCN	rt	0.33	**2c** (96) **3** (94)
6	**1a**	$(BrCH_2)_2CHOH$ (1.5)	MeCN	rt	0.5	**2d** (83) **3** (90)
7	**1a**	Ph_2CHOH (1.5)	MeCN	rt	0.33	**2e** (73) **3** (79)
8	**1a**	(±)-PhCH(Me)OH (1.5)	MeCN	rt	1.0	**2f** (51) **3** (88) **4** (21) **5** (5)
9	**1a**	(±)-PhCH(Me)OH (3.0)	MeCN	rt	2.0	**2f** (50) **3** (100) **4** (35) **5** (7)
10	**1a**	(±)-PhCH(Me)OH (5.0)	MeCN	rt	2.0	**2f** (48) **3** (96) **4** (40) **5** (4)
11	**1b**	(±)-PhCH(Me)OH (1.5)	MeCN	rt	0.5	**2f** (56) **4** (12) **5** (10) **6** (28)
12	**1b**	(±)-PhCH(Me)OH (1.5)	MeCN	−30	18	**2f** (63) **4** (16) **6** (20)
13	**1a**	(−)-Menthol (1.0)	MeCN	rt	1.0	— **3** (62) **4** (26) **5** (17)

[a] Isolated yield based on selenonium salt **1**.

Table 2 The reactions of alkenylselenonium salts with acyclic secondary alcohols[a]

Entry	7	ROH	Temp./°C	Time/min	2 (% yield)[b]
1	**7a**	(+)-PhCH(Me)OH	−30	30	**2g** (91)
2	**7b**	(+)-PhCH(Me)OH	0	30	**2g** (62)
3	**7b**	(+)-PhCH(Me)OH	−30	30	**2g** (65)
4	**7a**	(+)-$ClCH_2CH_2CHPhOH$	−30	120	**2h** (88)
5	**7a**	$(BrCH_2)_2CHOH$	−30	30	**2d** (91)
6	**7a**	Ph_2CHOH	−30	30	**2e** (90)

[a] Conditions: 1 equiv. of selenonium salt **7**, 1.1 equiv. of an alcohol and NaH in MeCN. [b] Isolated yield based on selenium salt **7**.

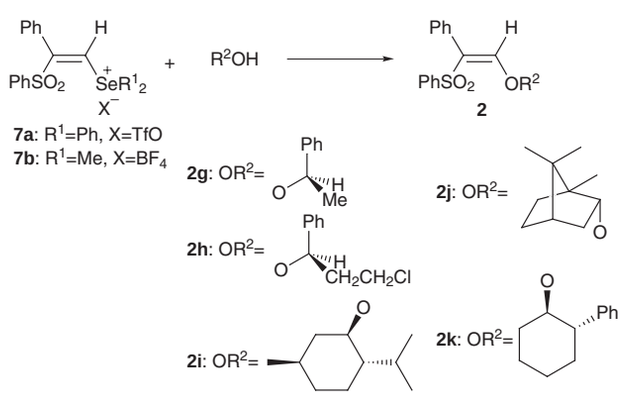
Table 3 The reactions of alkenylselenonium salts with cyclic secondary alcohols[a]

Entry	7 (equiv.)	ROH (equiv.)	Base	Solvent	Temp./°C	2 (% yield)
1	**7a** (1)	(−)-Menthol (1.5)	NaH	MeCN	−30	**2i** (39)[b]
2	**7a** (1)	(−)-Menthol (2.0)	NaH	MeCN	−30	**2i** (47)[b]
3	**7b** (1)	(−)-Menthol (1.2)	NaH	MeCN	−30	**2i** (29)[b]
4	**7b** (1.5)	(−)-Menthol (1)	NaH	MeCN	−30	**2i** (58)[c]
5	**7b** (3.0)	(−)-Menthol (1)	NaH	MeCN	−30	**2i** (67)[c]
6	**7b** (1.0)	(−)-Menthol (1)	PhLi	THF	−78	**2i** (64)[c]
7	**7b** (1.5)	(−)-Menthol (1)	PhLi	THF	−78	**2i** (80)[c]
8	**7b** (1.5)	(−)-Borneol (1)	PhLi	THF	−78	**2j** (96)[c]
9	**7b** (1.5)	(−)-*trans*-2-Phenylcyclohexan-1-ol	PhLi	THF	−78	**2k** (90)[c]

[a] These reactions were carried out for 12 h. [b] Isolated yield based on selenonium salt **7**. [c] Isolated yield based on alcohols.

11 and 12), although demethylation of **1b** occurred to afford alkynyl selenide **6**. Only single geometrical isomers of **2** were formed from the reactions. The stereochemistry of **2** was determined as (*Z*) by NOE measurement of **2d**.

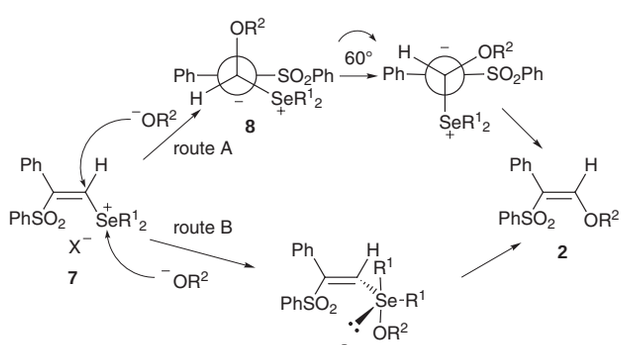
Next, we examined the reactions of alkenylselenonium salts **7**,[11a] which were intermediates of the reaction of alkynylselenonium salts with sodium benzenesulfinate and alcohols, with bulky secondary alkoxides (Scheme 2, Table 2). The reaction of



Scheme 2

diphenylalkenylselenonium salt **7a** with (+)-1-phenylethanol as an acyclic secondary alcohol in the presence of NaH at −30 °C for 30 min only gave an *O*-alkyl enol ether **2g** in high yield (entry 1). The reactions of dimethylalkenylselenonium salt **7b** afforded the desired product in 65% yield (entries 2 and 3). The reaction with (+)-3-chloro-1-phenylpropan-1-ol gave *O*-alkyl enol ether **2h** in 88% yield (entry 4). The reactions of **7a** with achiral secondary alcohols gave better results than those of diphenylalkynylselenonium salt **1a** (compare entries 5 and 6 in Table 2 with entries 6 and 7 in Table 1).

According to this procedure, we prepared the *O*-cycloalkyl enol ethers which had not been obtained from the reaction of alkynylselenonium salt **1a** (Scheme 2, Table 3). The reaction of diphenylalkenylselenonium salt **7a** with 1.5 equiv. of menthol in the presence of NaH gave the desired compound **2i** in low yield (entry 1). The yield of the reaction was increased up to 47% by use of 2 equiv. of alkoxide (entry 2). The reaction of dimethylalkenylselenonium salt **7b** and 1.2 equiv. of menthol with NaH afforded **2i** in only 29% yield (entry 3). The reason for the low yield was that menthol did not completely react with NaH and the unreacted NaH decomposed **7b**. The yields of **2i** were improved up to 67% by the use of excess selenonium salt **7b** (entries 4 and 5). We used PhLi as a base for the effective deprotonation of menthol. The reaction of 1.5 equiv. of **7b** with lithium menthoxide in THF at −78 °C afforded the desired product **2i** in 80% yield (entry 7). Similarly the reactions with bulky secondary cyclic alcohols, (−)-borneol and (−)-*trans*-2-phenylcyclohexan-1-ol gave *O*-alkyl enol ethers in excellent yields (entries 8 and 9). The products obtained from these reactions were all *Z*-isomers. A plausible mechanism for the reaction of alkenylselenonium salts with alkoxides is proposed on the basis of our previous investigations [11a] (Scheme 3). Route A



Scheme 3

proceeds *via* alkoxide ion addition to **7** to form betaine **8** and the subsequent elimination of a selenide leads to the *O*-alkyl enol ether **2** with retention of configuration.[11a,12] An alternative route involves the formation of the selenurane intermediate **9** followed by the ligand coupling between the alkoxy group and the alkenyl carbon.[11b,13] Both pathways are feasible explanations for the stereochemical outcome observed in these reactions. Thus we succeeded in the development of facile, efficient and stereoselective one-step synthesis of chiral (*Z*)-*O*-alkyl enol ethers from alkenylselenonium salts and chiral alcohols.

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Communication 9/05265H