

A Stereoselective Synthesis of Substituted Allyl Alcohol by Three-component Reaction of Acetylenic Sulfone, Phenylselenomagnesium Bromide and Ketones

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Abstract: Phenylseleno and sulfonyl substituted allyl alcohols were synthesized stereoselectively by the three-component reaction of acetylenic sulfone, phenylselenomagnesium bromide and ketones in one-pot.

Keywords: Acetylenic sulfone, ketone, allyl alcohol, stereoselectivity.

Substituted allyl alcohols are useful intermediates in organic synthesis, for example, they can be hydrogenated or isomerized to aldehydes enantioselectively¹. Substituted allyl alcohols are usually prepared based on Reformatsky reaction of the corresponding ketones or Horner-Wadsworth-Emmons reaction but a mixture of isomers is often obtained². Michael addition is acknowledged as useful tool for constructing complex organic molecules and is widely applied in organic synthesis³. But the electrophile, which are used to capture the products of the Michael addition, are mainly aldehydes⁴. Recently, we have reported the synthesis of substituted allyl alcohols from the Michael-aldol tandem reaction of acetylenic sulfone, magnesium selenolate and aldehydes⁵. As an extension of our research, we would like to report herein the high stereoselective synthesis of substituted allyl alcohol from the three-component reaction of acetylenic sulfone, phenylselenomagnesium bromide and ketone.

The three-component reaction of acetylenic sulfone **1**, magnesium selenolate **2** and aliphatic ketone **3** in THF/CH₂Cl₂ at -20°C to affords the substituted allyl alcohol **4** as the final product (**Scheme 1**). The results are summarized in **Table 1**.

However, when acetophenone was used, no expected tandem adduct was obtained from the three-component reaction of acetylenic sulfone **1**, magnesium selenolate **2** and acetophenone. This may due to the stereo effect because acetophenone is more crowded than aliphatic ketones.

All the products were characterized by ¹H NMR, ¹³C NMR, IR, EIMS and elemental analysis. The configuration of compound **Z-4** was deduced from that of (*Z*)-6-phenyl-

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seleno-5-(*p*-tolylsulfonyl)-4-methyl-5-undecen-4-ol (**Z-4b**), which was confirmed by NOESY spectrum.

Scheme 1

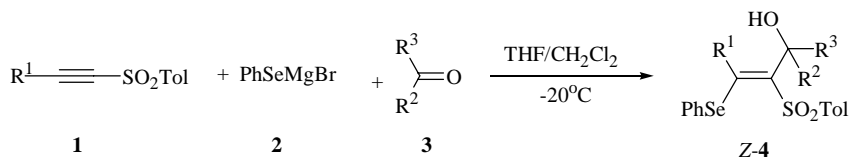


Table 1 Three-component reaction of acetylenic sulfones with phenylselenomagnesium bromide and aliphatic ketones^a

entry	R ¹	R ²	R ³	time (h)	yield of Z-4 (%) (<i>Z/E</i>) ^b
1	Ph	CH ₃	<i>n</i> -C ₃ H ₇	3	70 (Z-4a , 95/5)
3	Ph	-(CH ₂) ₅ -	<i>n</i> -C ₃ H ₇	3.5	65 (Z-4b , 96/4)
5	Ph	CH ₃	CH ₃ CH ₂	3	69 (Z-4c , 95/5)
2	<i>n</i> -C ₅ H ₁₁	CH ₃	<i>n</i> -C ₃ H ₇	3	79 (Z-4d , 96/4)
4	<i>n</i> -C ₅ H ₁₁	-(CH ₂) ₅ -	<i>n</i> -C ₃ H ₇	3.5	81 (Z-4e , 95/5)

^a The reaction was carried out at -20°C by adding **1** (0.5 mmol), **2** (0.6 mmol) and **3** (0.5 mmol) simultaneously in THF/CH₂Cl₂ (v/v = 1/4). ^b Isolated yield. The ratio of *Z/E* was determined by 400 MHz ¹H NMR spectra

In conclusion, we synthesized substituted allyl alcohol conveniently by the three-component reaction of acetylenic sulfone, magnesium selenolate and aliphatic ketone. The method had the advantages of simple procedures, mild reaction conditions and high selectivity.

General Procedure: Acetylenic sulfone (0.5 mmol) and ketone (0.5 mmol) were added to a colorless solution of phenylselenomagnesium bromide (0.6 mmol) in THF/CH₂Cl₂ (v/v=1:4, 5 mL) at -20°C with stirring. The reaction mixture turned to a pale yellow solution, which was maintained stirring at -20°C for 3-3.5h. After usual workup, the desired tandem adduct **4** was obtained.

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