



Contents lists available at ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

2-(Phenylseleno)ethanesulfonamide as a novel protecting group for aniline that can be deprotected by a radical reaction

Nobuhiro Kihara*, Yuji Mitsuhashi, Makoto Sato, Shun-ichi Hirose, Erika Goudo, Yoshinori Uzawa, Natsumi Shirai, Sari Hamamoto, Ryo Iwasaki, Akane Fujioka

Department of Chemistry, Faculty of Science, Kanagawa University, 2946 Tsuchiya, Hiratsuka 259-1293, Japan

ARTICLE INFO

Article history:

Received 21 March 2016
Revised 23 April 2016
Accepted 2 May 2016
Available online xxx

Keywords:

2-(Phenylseleno)ethanesulfonamide
Tributyltin hydride
Radical deprotection
Chemoselectivity
Slow addition

ABSTRACT

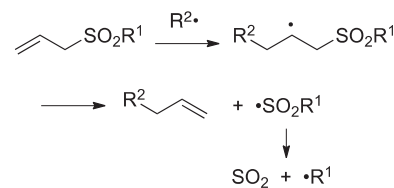
Anilines were protected as 2-(phenylseleno)ethanesulfonamide (SeES anilide) via sulfonylation by 2-chlorosulfonyl chloride followed by the conjugate addition of benzeneselenol. The SeES anilide was deprotected by radical reduction using tributyltin hydride in the presence of AIBN. The corresponding anilines were obtained in high yields when the hydride and AIBN were added to the system slowly. Since the radical reaction proceeds under neutral conditions, chemoselective deprotection of the SeES group was accomplished. The SeES anilide was stable under various conditions, including some severe conditions.

© 2016 Published by Elsevier Ltd.

Introduction

The protecting group of an amine is one of the most important tools in organic synthesis. The sulfonamide group has been considered as one of the most stable protecting groups of amines as it strongly resists both nucleophiles and electrophiles.¹ Because of the stability of the sulfonamide group, severe reaction conditions are necessary for their deprotection; therefore, their use has been limited in organic synthesis. Recently, novel sulfonamides that can be selectively deprotected under mild reaction conditions have been reported.² However, more efficient deprotection strategies are desired.

Radical reactions proceed under neutral conditions with high chemoselectivity. If sulfonamide could be deprotected by a radical reaction, it can be a potentially useful protecting group for an amine.³ Zard et al. reported that the 2-(alkylsulfonyl)ethyl radical produced from allylsulfone decomposes with the release of olefin and sulfur dioxide to form an alkyl radical (Scheme 1).⁴ Further, Moutrille and Zard reported the formation of amidyl radical from allylsulfonamide in the same manner.⁵ These reactions prompted us to develop a novel sulfonamide that can be deprotected by radical reduction. The β -radical of alkylsulfonamide produced from the abstraction of the phenylseleno group can be expected to



Scheme 1.

decompose to afford an aminyl radical that can be reduced to an amine.

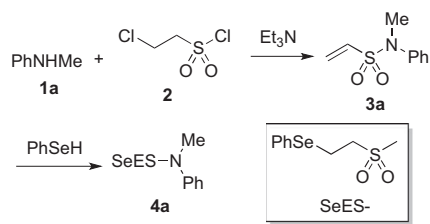
Results and discussion

N-Methylaniline **1a** was used as a precursor for the novel sulfonamide. Thus, **1a** was treated with 2-chloroethanesulfonyl chloride **2**, a cheap sulfonylation agent, in the presence of triethylamine to afford the vinylsulfonamide **3a**. The conjugate addition of benzeneselenol to **3a** afforded the 2-(phenylseleno)ethanesulfonamide (SeES amide) **4a** (Scheme 2). Both the reactions proceeded in high yield. The crude product of **3a** was analytically pure and could be used in the second step without further purification.

The radical deprotection of the SeES group was investigated. The reduction of **4a** was carried out using tributyltin hydride as the reducing agent to optimize the deprotection conditions. The addition of tributyltin hydride to the reaction system all at once

* Corresponding author. Tel.: +81 463 59 4111; fax: +81 463 58 9684.

E-mail address: kihara@kanagawa-u.ac.jp (N. Kihara).

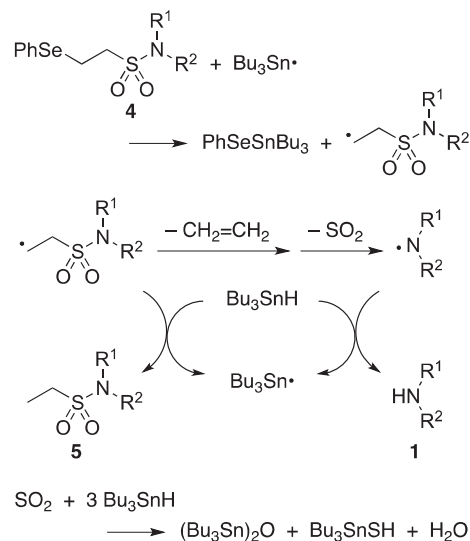


Scheme 2.

afforded ethanesulfonamide **5a** as the sole product. The primary radical produced by the abstraction of the phenylseleno group was trapped by tributyltin hydride before releasing ethylene. Therefore, it was deduced that the slow addition of tributyltin hydride was necessary to minimize the simple reduction. The solution of tin hydride and the initiator was added simultaneously to the reaction system over a period of 20 h. First, the reaction was attempted using 0.2 equiv of AIBN as the initiator. However, the result obtained under this condition was not very reproducible. The reproducibility improved with increasing amounts of AIBN. At least, 1 equiv of AIBN was necessary to obtain reproducible results. The yield of the reaction was maximum when 2 equiv of AIBN was used; the use of 3 equiv of AIBN decreased the yield. Therefore, 2 equiv of AIBN was used in further investigations.

The results are summarized in Table 1. The yield of **1a** significantly improved with increasing amounts of tributyltin hydride. At least 4 equiv of tributyltin hydride was necessary to afford **1a** in good yield. When the reaction was carried out at 60 °C, a significant amount of **5a** was produced. However, the yield decreased when the reaction was carried out at 100 °C, and the highest yield of **1a** was obtained when the reaction was carried out at 80 °C.

The possible reaction mechanism is shown in Scheme 3. The tributyltin radical abstracts the phenylseleno group to form the β -sulfonyl radical. When the concentration of tributyltin hydride was high, the β -sulfonyl radical was directly reduced by tributyltin hydride to afford **5**. When the concentration of tin hydride was kept to a minimum by slow addition, the reaction proceeded in an intramolecular fashion with the sequential release of ethylene and sulfur dioxide. High reaction temperatures are necessary because of the higher activation energy required for releasing ethylene from the primary radical. However, higher reaction temperatures decreased the efficiency of the radical initiator. The resulting



Scheme 3.

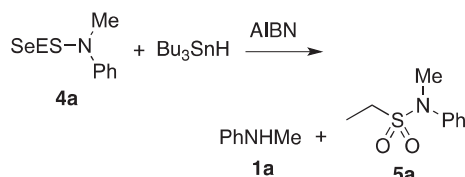
aminyl radical abstracts hydrogen from tributyltin hydride to afford amine **1**, and regenerates the tributyltin radical, thus completing the cycle. It was deduced that 1 equiv of tributyltin hydride was used for the reduction of the SeES group, whereas 3 equiv of tributyltin hydride was used for the reduction of the released SO₂. Because the resulting thiol (or tin sulfide) inhibited the radical reaction, an excess amount of AIBN was necessary to consume the radical scavengers.

One can suppose that benzeneselenol produced by the hydrolysis of PhSeSnBu₃ strongly inhibited the radical reaction. Thus, the radical reduction of *N*-methyl-2-(phenylthio)ethanesulfonamide, sulfur analogue of SeES amide **4a**, was examined. Because of less reactivity of the phenylthio group toward radical, higher temperature (160 °C) was necessary. However, excess initiator (6 equiv of di-*tert*-butyl peroxide) and excess Bu₃SnH (4 equiv) were also necessary to obtain **1a** in good yield (72%). These results indicate that SO₂ is the main source of radical scavenger although we cannot exclude the possibility that benzeneselenol inhibited the radical reaction in the case of **4a**.

To avoid using excess tin hydride, we examined other hydride sources such as triarylmethane, silanes, cyclohexadiene, benzothiazoline, and benzoxazoline. Triarylmethanes acted as the hydride sources. However, the best yield of **1a** was less than 10% when 4-methoxytriphenylmethane was used under xylene reflux condition. When tris(trimethylsilyl)silane⁶ (TMS₃SiH) was used, 65% of **1a** was obtained with 1 equiv of TMS₃SiH. Excess TMS₃SiH was unnecessary because TMS₃SiH did not reduce SO₂ although the efficiency and the reproducibility were lower than those of Bu₃SnH. Other hydride sources did not afford **1a** at all.

The radical deprotection of some SeES-protected amines **4** was investigated. The results are summarized in Table 2. The SeES group bound to the amino group of aniline derivatives was smoothly deprotected under the standard conditions. When the allyl group was introduced at the *ortho*-position (**4d** and **4e**), no radical cyclization product was observed although the system became complex, and the yields of the starting amines were lower. The SeES group could be selectively deprotected from **4g** even in the presence of the ester group because of the high chemoselectivity of the radical reaction under neutral conditions. Since aryl bromide and 1,4-phenylenediamine interfered with the radical reaction, the radical reduction of **4h** and **4i** was incomplete. In the case of **4h**, **1h** was obtained in lower yield while over-reduction product **1b** was observed only in the yield of 1%. When **4j** was

Table 1
Optimization of the reaction conditions for the deprotection of the SeES group^a



Bu ₃ SnH (equiv)	Temperature (°C)	Yield (%)	
		1a	5a
1.0	80	6	7
2.0	80	49	6
3.0	80	81	2
4.0	80	92	4
3.0	60	29	35
3.0	100	72	4
3.0	Reflux	55	4

^a Reactions were carried out in toluene. Bu₃SnH and AIBN were added dropwise over the period of 20 h.

Download English Version:

<https://daneshyari.com/en/article/5258906>

Download Persian Version:

<https://daneshyari.com/article/5258906>

[Daneshyari.com](https://daneshyari.com)