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Silver(I)-Catalyzed Deprenylation of Allylsulfonamide Derivatives

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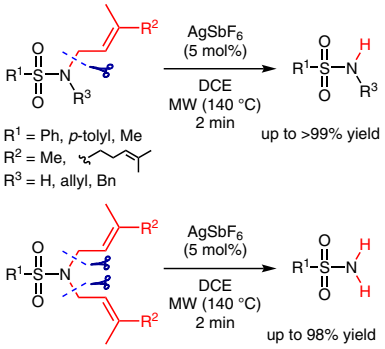

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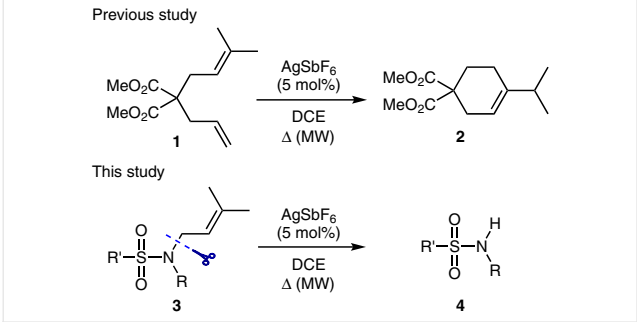
Abstract The silver(I)-catalyzed deprenylation of sulfonamide bearing prenyl functional groups on the nitrogen atom has been developed. In this reaction, the prenyl moiety was selectively eliminated without allyl or benzyl cleavage on the nitrogen atom. In addition, geranyl was also applicable for this elimination reaction. Furthermore, sulfonamide possessing two prenyl groups underwent a double deprenylation to form the corresponding deprenylated sulfonamide. Thus, a novel reactivity between the silver cation and double bond was observed.

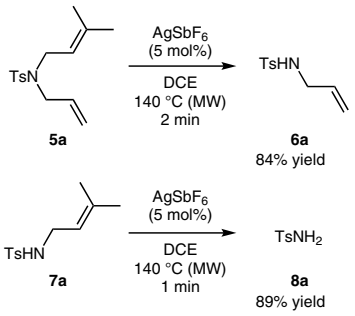
Key words C–N bond cleavage, silver, catalytic reaction, deprenylation, alkene

Since the discovery of the antibacterial drug, prontosil,[1] the sulfonamide moiety is widely accepted as one of the most important bioisosteres[2] of the carboxylic acid in medicinal chemistry. For further investigation regarding bioactive materials bearing the sulfonamide, a higher level of synthetic methods is required. Although several types of protecting groups for sulfonamide, such as *tert*-butyl,[3–5] functionalized benzyl,[6–11] and allyl[12–14] are already known, the selective deprotection processes (C–N bond cleavage) are still limited. On the other hand, silver salts are used for the catalytic reactions with alkynes due to the alkynophilicities.[15–18] Silver-ion chromatography is also well-known for separating lipids containing double bonds.[19–22] With regard to the principle of this separation, the silver-ion complexes with the double bonds.[23,24] However, interestingly, silver-catalyzed reactions with alkenes are limited.[25,26] Based on this information, we recently developed[27] the silver(I)-catalyzed cycloisomerization of a diene **1** involving alkyl rearrangements to form a cyclic product **2** (Scheme 1). Thus, it seemed that silver coordination with the double bond has the potential for causing additional reaction modes. We now report the selective deprenylation of allylsulfonamide **3** using a catalytic amount of $AgSbF_6$.



Scheme 1 Silver(I)-catalyzed reaction of olefins

After several examinations, we found that the selective deprenylation reaction of *N*-allyl-*N*-prenyl-*p*-toluenesulfonamide (**5a**) with 5 mol% of $AgSbF_6$ in DCE at 140 °C (microwave irradiation) for two minutes gave *N*-allyl-*p*-toluenesulfonamide (**6a**) in 84% yield (Scheme 2). More recently, Jirgensons[14] reported the same reaction using 6.5 equivalents of TFA and 6 equivalents of Et_3SiH in CH_2Cl_2 at room temperature for 60 minutes to afford **6a** in 68% yield.[28] Although our reaction conditions required a higher temperature, the chemical yields and reaction time were better. Also, an excess amount of a cation scavenger, such as Et_3SiH, was not required for our reaction, which must be another benefit. In addition, they reported that the deprenylation reaction of *N*-prenyl-*p*-toluenesulfonamide (**7a**) led to a complex mixture, whereas our reaction gave the tosylamide **8a** in 89% yield.



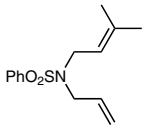
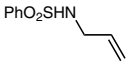
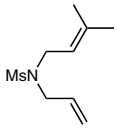
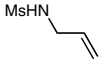
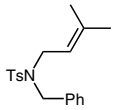
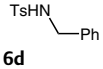
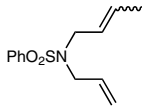
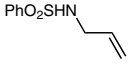
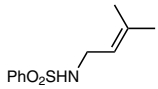
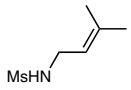
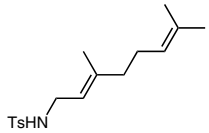
Scheme 2 Silver(I)-catalyzed deprenylation

Our next effort focused on the exploration of the scope and limitations. These results are summarized in Table 1. Selective deprenylation between the prenyl and allyl moieties smoothly occurred in not only the tosylamide **5a** but also for the benzenesulfonamide **5b** and mesylamide **5c** affording **6b** (88%) and **6c** (82%) in high yields (Table 1, entries 1 and 2). Substrate **5d** bearing prenyl and benzyl groups provided the deprenylation product **6d** in 69% yield without debenzylation (Table 1, entry 3). Jirgensons and co-workers[14] reported that the reaction of **5d** using TFA and Et_3SiH did not afford **6d**, thus the difference in the reactivities between both conditions must be clarified. Although elimination of the 2-butenyl group from substrate **5e** required a higher temperature (180 °C), the allylsulfonamide **6b** was observed in a modest yield (Table 1, entry 4). For the deprenylation using monoprenyl substrates **7b**,**c**, the corresponding benzenesulfonamide (**8b**) and mesylamide (**8c**) were obtained in good yields (Table 1, entries 5 and 6). A similar type of deallylation also occurred using the geranyl group instead of the prenyl group. Actually, the tosylamide **8a** (82%) was observed from the *N*-geranyl substrate **7d** (Table 1, entry 7). Although other silver salts ($AgBF_4$, AgOAc, etc.) were examined in several substrates, satisfied results were not observed (0–31% yield). In addition, heating conditions without silver salt did not afford the desired product.

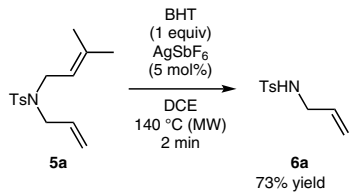
To elucidate the mechanism in detail, an efficient radical inhibitor, butylated hydroxytoluene (BHT), was applied to the deprenylation reaction (Scheme 3). When the diene **5a** was treated with one equivalent BHT and 5 mol% $AgSbF_6$, the deprenylated product **6a** was observed in 73% yield (84% without BHT), which encouraged us to consider that the main reaction proceeded without a free-radical mechanism.

Based on these results, the plausible mechanisms of deprenylation are shown in Scheme 4. Coordination with both the prenyl double bond and sulfonyl moiety of substrate **3** would form complex **A**. When the addition of the sulfonamide to the cationic silver produces intermediate **B**, deprotonative elimination at the prenyl group should provide the deprenylated intermediate **C**. In parallel, the double bond of

Table 1 Silver(I)-Catalyzed Monodeallylation of Allylsulfonamide

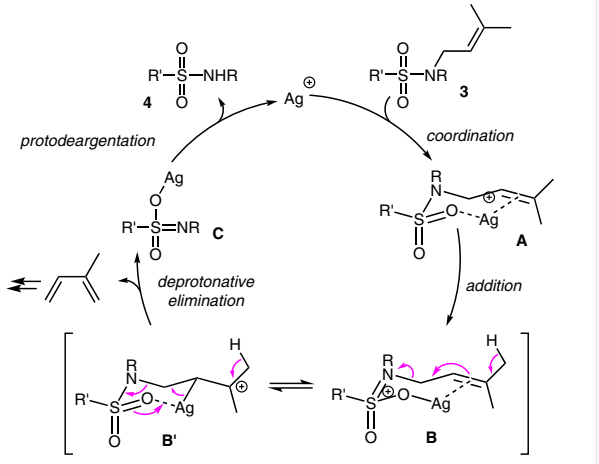
Entry	Substrate	Product	Yield (%)[a]
1	 **5b**	 **6b**	88
2	 **5c**	 **6c**	82[b]
3	 **5d**	 **6d**	69
4	 **5e** (mixture of *E*/*Z* = 3:1)	 **6b**	46[c]
5	 **7b**	PhO_2SNH_2 **8b**	78
6	 **7c**	$MsNH_2$ **8c**	quant.
7	 **7d**	$TsNH_2$ **8a**	82

[a]Substrate was reacted with 5 mol% $AgSbF_6$ in DCE at 140 °C (MW) for 2 min.
[b]Reacted for 80 s.
[c]Reacted at 180 °C using oil bath for 30 min.



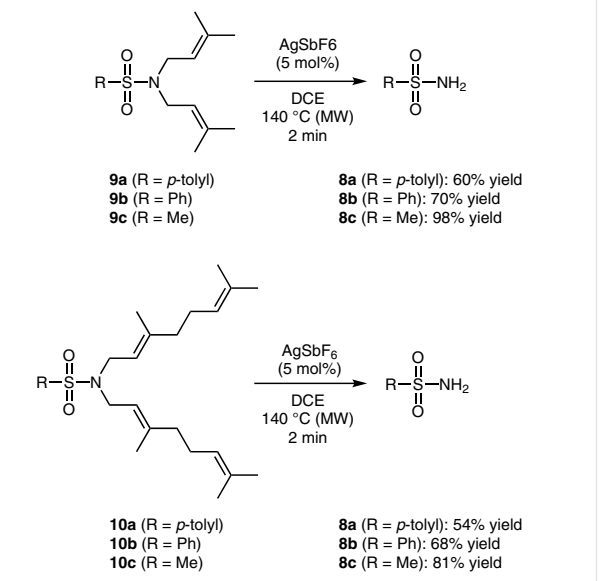
Scheme 3 Addition of radical scavenger

the prenyl part is also a candidate for the addition to the silver cation, which would form complex **B′**. Intermediates **B** and **B′** might be present in equilibrium. The common deprenylated complex **C** would then be constructed by the deprotonation and [3,3]-sigmatropic rearrangement of **B′**. Finally, the protodeargentation from **C** could form the corresponding products **4**.



Scheme 4 Plausible mechanisms

Based on the speculated mechanisms requiring the prenyl moiety and sulfonamide, another substitution group R on the nitrogen atom must not be directly involved in the deprenylation reaction. In other words, if the R group has a prenyl functionality, R would also be eliminated. Thus, the double deprenylation reaction was finally examined. As shown in Scheme 5, conversions of the bisprenyl sulfonamides **9a–c** bearing *p*-tolyl, phenyl, and methyl groups into the corresponding sulfonamides **8a–c** successfully proceeded in good yields. In addition, the bisgeranyl functionalities on the nitrogen of the sulfonamides **10a–c** were also possible to be eliminated. The resulting sulfonamides **8a–c** were observed in 54, 68, and 81% yield, respectively.



Scheme 5 Silver(I)-catalyzed double deprenylation

In summary, we developed the silver(I)-catalyzed selective deprenylation of the sulfonamide possessing allyl functional groups on the nitrogen atom.[28,29] This C–N bond cleavage simply proceeded by adding only a catalytic amount of $AgSbF_6$ at high temperature, and other reagents, such as an excess amount of a cation scavenger, were not required. In addition, the prenyl elimination selectively occurred without allyl or benzyl cleavage on the nitrogen atom. The geranyl group was also an active functionality for this elimination reaction. Furthermore, the double deprenylation of bisprenyl sulfonamide was also possible. Thus, we determined the novel reactivity between the silver cation and double bond. Further examinations using the silver catalyst and alkenes are currently under way.

Acknowledgment

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Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/s-0036-1589066.

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(28) **General Procedure for Deprenylation**
To a solution of substrate (0.10 mmol) in DCE (0.5 mL) was added a solution of $AgSbF_6$ (0.005 mmol) in DCE (0.5 mL) under an atmosphere of N_2. After stirring for 2 min at 140 °C under microwave irradiation, the solvent was evaporated off. The residue was chromatographed with hexane/EtOAc to afford the deprenylated sulfonamide.
(29) **Analytical Data for 6a**[30]
Compound **6a** was a yellow solid: IR 3281, 1323, 1158, 1093, 814, 666, 550 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ = 7.76 (d, 2 H, *J* = 8.1 Hz), 7.31 (d, 2 H, *J* = 8.1 Hz), 5.76–5.69 (m, 1 H), 5.19–5.15 (m, 1 H), 5.11–5.09 (m, 1 H), 4.53 (br t, 1 H, *J* = 5.8 Hz), 3.60–3.58 (m, 2 H), 2.43 (s, 3 H). ^{13}C NMR (151 MHz, $CDCl_3$): δ = 143.5, 136.9, 132.9, 129.7, 127.1, 117.7, 45.8, 21.5.
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