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A radical cascade reaction of aza-1,6-enyne compounds using allyltributyltin

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ABSTRACT

The radical cascade reaction of allyltin with aza-1,6-enyne compounds was studied. Optically active aza-1,6-enynes underwent a radical cascade process in the presence of a high concentration of allyltributyltin to give stannolanes as the major isomer. Piperidines were also observed in small amounts when an allylic unit was introduced stereoselectively to the *trans*-position of the aryl group at the C2 position. The yield of the products dramatically decreased with concentrations of tin reagent. The E/Z selectivity at the exomethylene group in piperidine depended on the reaction temperature, and it almost doubled when the reaction was carried out at 30 °C. In this study, the reaction mechanism of the radical cascade is discussed.

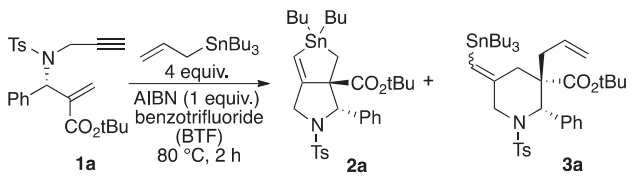
1. Introduction

Radical reactions occupy an important position in organic chemistry.[1] Radical cascades are those in which the key step constitutes a radical reaction and they provide a useful route for the preparation of carbocyclic and heterocyclic compounds through radical cyclization reactions.[2] Recently, we reported an interesting radical cascade with 1,6-enyne compounds[3] wherein a tin radical underwent a radical addition–cyclization–direct substitution (S_Hi)[4] reaction to give high yields of bicyclic stannolanes;[5] stereoselectivity was very high during the cyclization process. We also estimated the kinetic parameter of the direct substitution reaction on a tin atom.[6] A radical cascade reaction of similar compounds was reported by Kim and Shanmugam, but they did not observe any stannolane formation.[7] They reported that the radical cascade reaction of oxy-1,6-enynes gave tetrahydropyrane derivatives. Additionally, Kim reported that aza-1,6-enynes underwent cyclization triggered by allyltributyltin to give piperidine in moderate yields.[8] This contradicted our findings, which showed that the same aza-1,6-enynes resulted in an exclusive formation of stannolanes by treatment with Bu_3SnH.[5]

The present study aims to understand the differences in these results and investigate the reactions that occur in the presence of allyltin compounds. We disclose that aza-1,6-enynes undergoes radical cascade process to mainly give stannolanes, and piperidine formation occurs as a minor process. As the E/Z ratios depends on the reaction temperature, we believe that the reaction progressed through the addition of tin radical to the α,β-unsaturated end followed by cyclization reaction with the terminal alkyne unit to give an intermediate vinyl radical that attacks the tin atom to give stannolane or an alkyl radical intermediate. The product ratio between stannolane and piperidine reflects a rough ratio between radical substitution reaction in tin from back-side and front-side modes.

2. Results and discussion

We first examined the reaction of compound **1a** with allyltributyltin at various concentrations (Scheme 1). The results are summarized in Table 1.



Scheme 1. Reaction of 1a with allyltributyltin.

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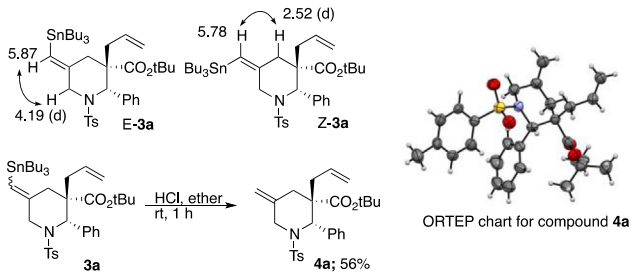
0040-4020/

Table 1
Radical cascade reaction of **1a** with allyltributyl tin

Entry	Solvent[b]	Conc. (M)	**2a**; Yield (%)[a]	**3a**; Yield (%)[a]	**2a**/**3a**	**3**; E/Z[a]	**1a**; Recovery (%)[a]
1	—	3.2	47 (49)	26 (15)	1.8	51/49	0
2	BTF	1.0	50	19	2.6	53/47	0
3	BTF	0.8	51	30	1.7	52/48	0
4	BTF	0.3	18	9	2	50/50	46
5	BTF	0.1	5.4	1.5	3.6	59/41	75

[a] NMR yields estimated by ^{1}H NMR integration. Isolated yields are in parentheses.
[b] BTF=$CF_3C_6H_5$.

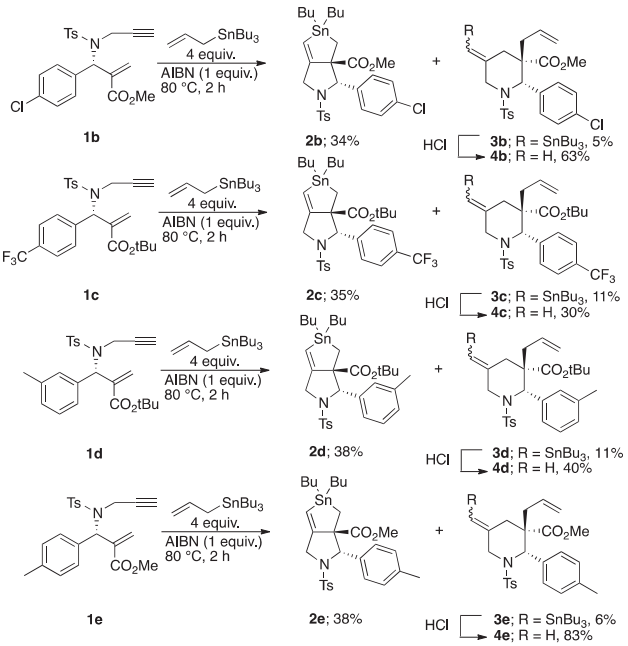
The aza-1,6-enyne **1a** underwent radical cascade reaction on treatment with allyltributyltin under no solvent conditions at 80 °C (entry 1). The starting material was consumed smoothly and two major products were formed. One was stannolane **2a** that was obtained in 47% yield. The structure of **2a** was determined by comparison with an authentic sample prepared in our previous method.[5] It is noteworthy that stannolane **2a** was isolated as a single isomer and the other stereoisomer was not observed in the reaction mixture. The other product **3a** was also isolated in 26% by purification using a recycle GPC apparatus. It was a mixture of *E*/*Z* isomers whose ratio was approximately 1:1. This diastereomeric difference was caused by the difference in the configuration at the exo-methylene unit and not by the stereochemistry of the piperidine ring. The stereochemistries of *E*-**3a** and *Z*-**3a** were determined by the NOESY spectra, where a cross peak between 5.87 (Sn−CH=) and 4.19 (−NCH_2−) was observed in *E*-**3a** whereas a cross peak between 5.78 (Sn−CH=) and 2.52 (−CH_2_C(CO_2R)−) was observed in *Z*-**3a**. The *E*/*Z* ratio slightly improved when the reaction was performed under lower concentration conditions (entry 5). The tributyltin group was removed by an acidic treatment to give exomethylene piperidine **4a**, the structure of which was unambiguously determined by X-ray crystallographic analysis (Scheme 2).[9]



Scheme 2. Structural elucidation of piperidine 3a and 4a.

As yield of **2a** and **3a** decreased with concentration of allyltributyltin. For example, the yields of **2a** and **3a** were 50% and 19% yield, respectively, when the reaction was performed at 1 M concentration whereas the yields dropped down to 5.4% and 1.5%, respectively, when **1a** was treated at 0.1 M concentration (entries 2 and 5). At low concentration (0.1 M), the percentage recovery of compound **1a** was 75%. This was contrary to the result obtained during the reaction of **1a** with Bu_3SnH, where the yield of stannolane **2a** was 80%.[5] However, the product ratios between **2a** and **3a** were not affected by reaction conditions; the values ranged between 1.7 and 3.6, and their average was calculated to be 2.3.

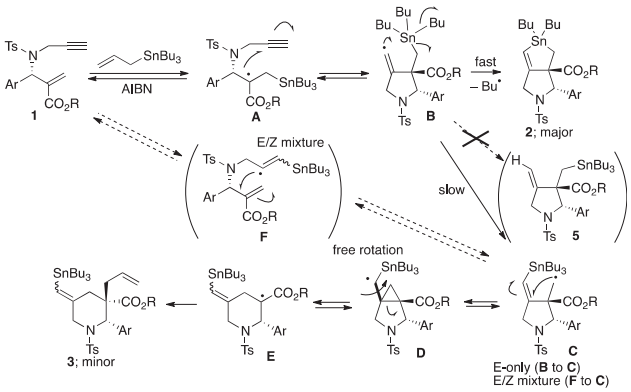
The results obtained in our study were found to be significantly different from those reported by Kim et al., in which they obtained exomethylene piperidines at yields higher than 60%.[8] To validate our results, we examined the reaction of various aza-1,6-enyne substrates **1** under similar reaction conditions. The results are summarized in Scheme 3. The reaction was performed under no solvent conditions.



Scheme 3. The reaction of allyltributyltin with various aza-1,6-enynes 1.

Our results clearly show that stannolane **2**, which was always obtained as a single diastereomer, was the main products when 1,6-enyne **1** was exposed to allyltributyltin. The yield of piperidine **3** was around 10%, indicating its formation was only a minor process. The Bu_3Sn group in piperidines **3** was readily removed by treatment with a concentrated aqueous HCl to give compound **4**.

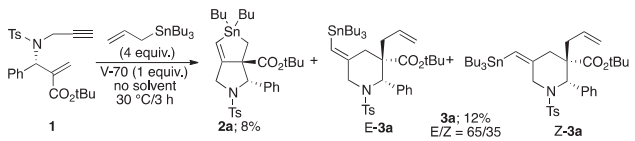
From all the abovementioned results, the reaction mechanism is proposed as shown in Scheme 4. The precursor **1** undergoes a radical addition of the tin radical to give an intermediate **A** which then attacks the terminal alkyne unit in 5-exo-dig mode, leading to the formation of a vinyl radical **B**. The intermediate **B** can undergo two possible reaction pathways; one is the radical substitution reaction to produce butyl radical and stannolane **2**, and the other is the radical substitution reaction to give a CH_2 radical **C**. The former pathway is believed to be a fast reaction step because its kinetic parameter was estimated to be around 4.23×10^8 s^{-1}.[6] Thus, most of the radical **B** gives stannolane **2**. However, there is no source of hydrogen to trap **B** in order to give the exomethylene product **5**; therefore radical **B** has a chance of undergoing the latter reaction pathway to give radical **C** by the S_Hi process in retention configuration, which is a relatively slower



Scheme 4. The reaction pathway.

process. The radical substitution reaction from **B** to **C** is believed to be irreversible because radical **C** is alkyl radical in nature and hence thermodynamically more stable than the vinyl radical **B**.[10] Once radical **C** is formed, a rearrangement through cyclopropylmethyl radical **D** progresses to give piperidine radical **E**, which is trapped by the allyl group of allyltributyltin to give the tin radical and product **3**. There is another possibility for the formation of radical **C** through radical **F**, which is formed by radical addition to the terminal alkyne unit. However, this is less likely to occur because the addition of a tin radical to an α,β-unsaturated ester is much faster than the addition to an alkyne unit.[11] Also, it is very difficult to produce product **2** through this route, which is the major product of the reaction. In all the radical cascade reactions of 1,6-enynes **1**, we observed the addition occurred exclusively from the α,β-unsaturated ester unit and not from the alkyne unit.

To check the abovementioned assumption, we examined the same reaction at 30 °C, and found that the *E*/*Z* ratio of **3a** improved to 65/35 although the total yields of **2a** and **3a** decreased (Scheme 5). Thus, *E*-**3a** became a major product of the reaction as long as a low temperature reaction condition was employed. A similar result was observed in the reaction with Bu_2PhSnH.[6] We believe that the free rotation of the carbon−carbon single bond in intermediate **D** is suppressed under lower temperature conditions and *E*-**3a** should be the main product as long as the intermediate radical **C** is generated through radical substitution reaction of **B** to **C**. Conversely, if the intermediate radical **C** is formed through **F** to **C**, the formation of **3a** should occur in a non-stereoselective manner and not be affected by the change in reaction temperature.[12] This result supports the assumption that the intermediate radical is mainly produced from the radical substitution process of **B** to **C** and not from the radical cyclization of **F** to **C**.



Scheme 5. The reaction of 1a with allyltributyltin at 30 °C.

Finally, a rough kinetic estimation was performed for the S_Hi process in retention configuration, i.e., the process from radical **B** to **C**. Although the kinetic parameter for the radical substitution reaction of **B** to product **2** was already estimated to be 4.23×10^8 s^{-1}, this value was calculated at 30 °C, and therefore cannot be used to estimate and absolute value for the kinetic parameter of **B** to **C**. However, an average of the product ratios between **2a** and **3a** was found to be 2.3, which was unaffected by reaction conditions. Thus, we believe that the rate constant of the S_Hi process in retention configuration (**B** to **C**) should be 2.3 times smaller then that of the S_Hi process in inversion configuration (**B** to **2**). This is in good agreement with our previous results in which the radical cascade driven by $PhBu_2SnH$ produced a piperidine as a minor product.

3. Conclusion

In conclusion, the present study reveals the reaction pathway between aza-1,6-enynes and allyltributyltin, which made confusion because of inconsistent results reported in literature. It is clearly shown that the tin radical dominantly attacks from the α,β-unsaturated ester side and radical cascade reactions, including S_Hi process progresses, occurs. The product ratio gives a rough estimation of the difference in rate constants of the S_Hi process between the back-side attack (normal) and the front-side attacks. Although the yields of the piperidine were rather low, this investigation gives useful information about radical substitution reactions. Further work focused on the improvement of the piperidine synthesis in radical cascade is underway and will be reported in due course.

4. Experimental section

4.1. General

All ^1H and ^{13}C NMR spectra were recorded on JEOL lamda-500 or JNM-ECA 500 Delta2 (500 MHz for ^1H and 126 MHz for ^{13}C) spectrometer. Allyltributyltin was purchased from TCI. 1,6-enynes **1** were prepared by the previous reported method.[3] All the reactions in this paper were performed under nitrogen atmosphere unless otherwise mentioned. High resolution mass spectra (HRMS) were was measured by JEOL JMS T-100LP LC-ESI mass spectrometer.

4.2. The reaction of 1a with allyltributyltin (Table 1, entry 1)

A mixture of **1a** (212 mg, 0.50 mmol), allyltributyltin (662 mg, 2.00 mmol), and AIBN (81.8 mg, 0.50 mmol) was heated at 80 °C for 1 h. The reaction mixture was directly subjected flash chromatography (silica gel-K_2CO_3[13] 9:1/hexane then hexane-EtOAc 15:1 v/v) to give to **2a** in 49% yield (159 mg, 0.24 mmol) along with **3a** in 15% yield (57 mg, 0.075 mmol).

4.3. Conversion of 3a to 4a (Scheme 2)

A biphasic solution of **3a** (30.6 mg, 0.04 mmol) in ether (0.4 mL) and conc. HCl (0.04 mL) was stirred at room temperature for 1 h. Concentrated crude product was purified through flash chromatography (silica gel/hexane then hexane-EtOAc 10:1 v/v) to give **4a** in 58% yield (10.6 mg, 0.023 mmol).

Other compound **2** and **4** were prepared in a similar manner.

*4.3.1. (3S,3aS)-tert-Butyl 5,5-dibutyl-3-phenyl-2-tosyl-1,2,3,3a,4,5-hexahydrostannolo[3,4-c]pyrrole-3a-carboxylate (**2a**).* Colorless oil; $[\alpha]_D$ +7.7 (*c* 1.04, $CHCl_3$); ν_{max} (neat) 1720, 1367, 1348, 1161 cm^{-1}; δ_H (500 MHz $CDCl_3$) 7.41 (d, *J*=8.1 Hz, 2H), 7.20−7.09 (m, 3H), 7.06 (d, *J*=8.0 Hz, 2H), 6.97−6.90 (m, 2H), 6.55 (s, 1H), 5.44 (s, 1H), 4.15 (dd, *J*=12.9, 2.2 Hz, 1H), 4.01 (d, *J*=12.9 Hz, 1H), 2.31 (s, 3H), 1.51−1.42 (m, 2H), 1.37 (d, *J*=2.1 Hz, 9H), 1.29−1.19 (m, 4H), 1.13−0.95 (m, 6H), 0.90 (d, *J*=13.5 Hz, 1H), 0.83 (t, *J*=7.3 Hz, 3H), 0.73 (t, *J*=7.0 Hz, 3H), 0.23 (d, *J*=12.6 Hz, 1H); δ_C (126 MHz, $CDCl_3$) 173.8, 158.3, 142.6, 139.6, 136.6, 129.1 (2C), 128.1 (br, 2C), 128.1 (2C), 128.0, 127.5, 127.3 (2C), 81.6, 69.7, 68.6, 50.6, 29.0, 28.7, 27.8 (3C), 27.1, 27.0, 23.5, 21.5, 13.7, 13.1, 12.9, 12.3; HRMS (ESI-TOF, HCO_2Na): MNa^+, found 682.1975. $C_{32}H_{45}NNaO_4S^{120}Sn$ requires 682.1989.

*4.3.2. (2S,3S)-tert-Butyl 3-allyl-2-phenyl-5-methylene-1-tosylpiperidine-3-carboxylate (**4a**).* Colorless solid; mp 123.0−124.0 °C; $[\alpha]_D$ +23.3 (*c* 0.06, $CHCl_3$); ν_{max} (neat) 1730, 1370, 1223 cm^{-1}; δ_H (500 MHz $CDCl_3$) 7.29 (d, *J*=6.3 Hz, 2H), 7.25−7.11 (m, 5H), 6.97 (d, *J*=8.5 Hz, 2H), 5.66−5.51 (m, 1H), 5.13 (s, 1H), 5.12−5.03 (m, 3H), 4.93 (d, *J*=1.6 Hz, 1H), 4.15 (d, *J*=14.1 Hz, 1H), 3.63 (d, *J*=14.1 Hz, 1H), 2.92 (d, *J*=15.7 Hz, 1H), 2.67 (dd, *J*=14.2, 9.1 Hz, 1H), 2.54 (dd, *J*=13.6, 6.9 Hz, 1H), 2.47 (d, *J*=15.4 Hz, 1H), 2.28 (s, 3H), 1.10 (s, 9H); δ_C (126 MHz, $CDCl_3$) 171.8, 142.7, 137.5, 137.1, 136.2, 132.6, 130.0 (2C), 129.0 (2C), 128.2 (2C), 128.0, 127.2 (2C), 119.3, 114.2, 81.4, 77.4, 63.0, 50.5, 47.2, 40.7, 32.1, 27.6 (3C), 21.4; HRMS (ESI-TOF, HCO_2Na): MNa^+, found 490.2023. $C_{27}H_{33}NNaO_4S$ requires 490.2028.

*4.3.3. (3S,3aS)-Methyl 5,5-dibutyl-3-(p-chlorophenyl)-2-tosyl-1,2,3,3a,4,5-hexahydrostannolo[3,4-c]pyrrole-3a-carboxylate (**2b**).* Colorless oil; $[\alpha]_D$ +16.7 (*c* 1.03, $CHCl_3$); ν_{max} (neat) 1728,

1348, 1161 cm^{-1}; δ_H (500 MHz $CDCl_3$) 7.51 (d, *J*=7.7 Hz, 2H), 7.17 (d, *J*=7.2 Hz, 2H), 7.15 (d, *J*=7.7 Hz, 2H), 6.94 (d, *J*=7.8 Hz, 2H), 6.63 (s, 1H), 5.39 (s, 1H), 4.14–4.05 (m, 2H), 3.44 (s, 3H), 2.37 (s, 3H), 1.53–1.33 (m, 2H), 1.30–0.96 (m, 10H), 0.90 (d, *J*=12.9 Hz, 1H), 0.83 (t, *J*=7.3 Hz, 3H), 0.76 (t, *J*=7.1 Hz, 3H), 0.16 (d, *J*=13.1 Hz, 1H); δ_C (126 MHz, $CDCl_3$) 174.8, 157.2, 143.1, 138.5, 136.0, 133.5, 129.5, 129.4–129.3 (m, 2C), 129.3 (2C), 128.4 (2C), 127.5 (2C), 68.9, 67.9, 52.8, 50.6, 28.9, 28.8, 27.1, 27.0, 21.5, 13.7, 13.7, 13.7, 13.1, 12.5; HRMS (ESI-TOF, HCO_2Na): MNa^+, found 674.1113. $C_{29}H_{38}ClNNaO_4S^{120}Sn$ requires 674.1130.

*4.3.4. (2S,3S)-Methyl 3-allyl-2-(4-chlorophenyl)-5-methylene-1-tosylpiperidine-3-carboxylate (**4b**).* Colorless solid; mp 158.0–159.0 °C; $[\alpha]_D$ −11.4 (*c* 0.14, $CHCl_3$); ν_{max} (neat) 1730, 1370, 1223 cm^{-1}; δ_H (500 MHz $CDCl_3$) 7.22 (d, *J*=8.1 Hz, 2H), 7.10 (d, *J*=8.1 Hz, 2H), 7.06 (dd, *J*=8.3, 1.9 Hz, 2H), 7.00 (d, *J*=7.0 Hz, 2H), 5.62–5.45 (m, 1H), 5.16 (s, 1H), 5.12–5.00 (m, 3H), 4.97 (q, *J*=1.8 Hz, 1H), 4.29 (dt, *J*=13.8, 1.4 Hz, 1H), 3.71 (d, *J*=13.9 Hz, 1H), 3.41 (d, *J*=1.4 Hz, 3H), 2.81 (dt, *J*=15.1, 2.0 Hz, 1H), 2.71–2.61 (m, 1H), 2.61–2.52 (m, 1H), 2.48 (d, *J*=15.2 Hz, 1H), 2.32 (s, 3H); δ_C (126 MHz, $CDCl_3$) 173.0, 143.2, 136.5, 135.7, 135.7, 134.1, 132.3, 130.6 (2C), 129.1 (2C), 128.3 (2C), 127.1 (2C), 119.6, 114.9, 62.2, 51.8, 51.1, 47.5, 39.8, 31.2, 21.5; HRMS (ESI-TOF, HCO_2Na): MNa^+, found 482.1177. $C_{24}H_{26}ClNNaO_4S$ requires 482.1169.

*4.3.5. (3S,3aS)-tert-Butyl 5,5-dibutyl-3-(p-trifluoromethylphenyl)-2-tosyl-1,2,3,3a,4,5-hexahydrostannolo[3,4-c]pyrrole-3a-carboxylate (**2c**).* Colorless oil; $[\alpha]_D$ +3.2 (*c* 1.06, $CHCl_3$); ν_{max} (neat) 1716, 1325, 1161 cm^{-1}; δ_H (500 MHz $CDCl_3$) 7.46–7.41 (m, 2H), 7.38 (d, *J*=7.8 Hz, 2H), 7.07 (d, *J*=7.9 Hz, 4H), 6.60 (s, 1H), 5.47 (s, 1H), 4.13 (d, *J*=12.4 Hz, 1H), 4.06 (d, *J*=12.9 Hz, 1H), 2.30 (s, 3H), 1.46 (q, *J*=8.0 Hz, 2H), 1.34 (s, 9H), 1.22 (dt, *J*=14.4, 7.1 Hz, 4H), 1.15–0.94 (m, 6H), 0.90 (d, *J*=13.1 Hz, 1H), 0.82 (t, *J*=8.2, 6.4 Hz, 3H), 0.69 (t, *J*=7.0 Hz, 3H), 0.09 (d, *J*=12.4 Hz, 1H); δ_C (126 MHz, $CDCl_3$) 173.3, 157.5, 144.0, 143.0, 136.2, 129.6 (q, *J*=32.5 Hz), 129.2 (2C), 128.8, 128.4 (m), 128.2, 127.2 (2C), 125.0 (q, *J*=3.7 Hz), 81.9, 69.5, 67.9, 50.7, 28.9, 28.7, 27.7 (3C), 27.1, 26.8, 23.4, 21.4, 13.7, 13.4, 13.2, 12.7, 12.2; HRMS (ESI-TOF, HCO_2Na): MNa^+, found 750.1872. $C_{33}H_{44}F_3NNaO_4S^{120}Sn$ requires 750.1863.

*4.3.6. (2S,3S)-tert-Butyl 3-allyl-2-(p-trifluoromethylphenyl)-5-methylene-1-tosylpiperidine-3-carboxylate (**4c**).* Colorless solid; mp 151.0–152.0 °C; $[\alpha]_D$ +10.4 (*c* 0.17, $CHCl_3$); ν_{max} (neat) 1724, 1325, 1161 cm^{-1}; δ_H (500 MHz $CDCl_3$) 7.42–7.31 (m, 4H), 7.25 (d, *J*=8.7 Hz, 2H), 6.99–6.93 (m, 2H), 5.63–5.52 (m, 1H), 5.17–5.04 (m, 4H), 4.96 (s, 1H), 4.27 (d, *J*=12.9 Hz, 1H), 3.65 (d, *J*=14.3 Hz, 1H), 2.83 (d, *J*=15.0 Hz, 1H), 2.65 (dd, *J*=14.8, 6.6 Hz, 1H), 2.54 (dd, *J*=14.3, 6.1 Hz, 1H), 2.50 (d, *J*=15.4 Hz, 1H), 2.27 (s, 3H), 1.11 (s, 9H); δ_C (126 MHz, $CDCl_3$) 171.4, 143.2, 141.0, 136.8, 135.8, 132.2, 130.2 (2C), 129.1 (2C), 127.0 (2C), 124.9 (2C, q, *J*=3.4 Hz), 122.9 (q, *J*=91.7 Hz), 122.8, 119.6, 114.8, 81.9, 62.5, 50.5, 47.5, 40.6, 31.9, 27.7 (3C), 21.3; HRMS (ESI-TOF, HCO_2Na): MNa^+, found 558.1899. $C_{28}H_{32}F_3NNaO_4S$ requires 558.1902.

*4.3.7. (3S,3aS)-tert-Butyl 5,5-dibutyl-3-(m-tolyl)-2-tosyl-1,2,3,3a,4,5-hexahydrostannolo[3,4-c]pyrrole-3a-carboxylate (**2d**).* Colorless oil; $[\alpha]_D$ +1.0 (*c* 1.27, $CHCl_3$); ν_{max} (neat) 1718, 1344, 1161 cm^{-1}; δ_H (500 MHz $CDCl_3$) 7.42–7.36 (m, 2H), 7.05 (d, *J*=8.0 Hz, 2H), 7.01 (d, *J*=7.8 Hz, 1H), 6.95 (d, *J*=7.6 Hz, 1H), 6.87–6.57 (m, 2H), 6.57–6.53 (m, 1H), 5.39 (s, 1H), 4.16 (dd, *J*=12.9, 2.2 Hz, 1H), 3.99 (d, *J*=12.9 Hz, 1H), 2.31 (s, 3H), 2.15 (s, 3H), 1.54–1.42 (m, 2H), 1.37 (s, 9H), 1.33–1.18 (m, 4H), 1.14–1.00 (m, 6H), 0.91 (d, *J*=12.8 Hz, 1H), 0.83 (t, *J*=7.4 Hz, 3H), 0.72 (t, *J*=7.1 Hz, 3H), 0.23 (d, *J*=13.5 Hz, 1H); δ_C (126 MHz, $CDCl_3$) 173.9, 158.5, 142.5, 139.3, 137.5, 136.6, 129.0 (2C), 128.8–128.4 (br), 128.2, 127.9, 127.8, 127.3 (2C), 125.3, 81.6, 69.7, 68.7, 50.7, 29.0, 28.6, 27.8 (3C), 27.1, 27.0, 21.4, 13.7, 13.5, 13.1, 12.9, 12.2; HRMS (ESI-TOF, HCO_2Na): MNa^+, found 696.2131. $C_{33}H_{47}NNaO_4S^{120}Sn$ requires 696.2146.

*4.3.8. (2S,3S)-tert-Butyl 3-allyl-2-(m-tolyl)-5-methylene-1-tosylpiperidine-3-carboxylate (**4d**).* Colorless solid; mp 125.0–126.0 °C; $[\alpha]_D$ +12.7 (*c* 0.22, $CHCl_3$); ν_{max} (neat) 1737, 1727, 1385, 1352, 1228, 1217, 1158 cm^{-1}; δ_H (500 MHz $CDCl_3$) 7.23 (d, *J*=8.2 Hz, 2H), 7.07 (d, *J*=7.4 Hz, 1H), 7.03–6.93 (m, 5H), 5.66–5.53 (m, 1H), 5.13–5.03 (m, 4H), 4.93 (s, 1H), 4.19 (d, *J*=14.0 Hz, 1H), 3.66 (d, *J*=13.3 Hz, 1H), 2.90 (d, *J*=15.3 Hz, 1H), 2.68 (dd, *J*=13.6, 8.5 Hz, 1H), 2.54 (dd, *J*=13.8, 5.1 Hz, 1H), 2.46 (d, *J*=15.3 Hz, 1H), 2.28 (s, 3H), 2.19 (s, 3H), 1.11 (s, 9H); δ_C (126 MHz, $CDCl_3$) 171.8, 142.6, 137.6, 137.5, 136.8, 136.2, 132.7, 131.1, 128.9 (2C), 128.6, 128.0, 127.2 (2C), 126.6, 119.2, 114.2, 81.3, 63.1, 50.6, 47.4, 40.6, 32.0, 27.7 (3C), 21.4, 21.4; HRMS (ESI-TOF, HCO_2Na): MNa^+, found 504.2182. $C_{28}H_{35}NNaO_4S$ requires 504.2185.

*4.3.9. (3S,3aS)-Methyl 5,5-dibutyl-3-(p-tolyl)-2-tosyl-1,2,3,3a,4,5-hexahydrostannolo[3,4-c]pyrrole-3a-carboxylate (**2e**).* Colorless oil; $[\alpha]_D$ +15.5 (*c* 1.20, $CHCl_3$); ν_{max} (neat) 1728, 1344, 1161 cm^{-1}; δ_H (500 MHz $CDCl_3$) 7.50 (d, *J*=7.9 Hz, 2H), 7.13 (d, *J*=7.9 Hz, 2H), 6.98 (d, *J*=7.7 Hz, 2H), 6.87 (d, *J*=7.6 Hz, 2H), 6.60 (s, 1H), 5.38 (s, 1H), 4.13 (dd, *J*=13.0, 2.1 Hz, 1H), 4.09 (d, *J*=14.2 Hz, 1H), 3.43 (s, 3H), 2.35 (s, 3H), 2.27 (s, 3H), 1.71 (s, 2H), 1.42 (dp, *J*=16.6, 8.6, 8.0 Hz, 2H), 1.28–0.95 (m, 8H), 0.90 (d, *J*=13.1 Hz, 1H), 0.82 (t, *J*=7.4 Hz, 3H), 0.74 (t, *J*=7.0 Hz, 3H), 0.25 (d, *J*=13.0 Hz, 1H); δ_C (126 MHz, $CDCl_3$) 175.1, 157.8, 142.7, 137.2, 136.8, 136.2, 129.1 (2C), 128.9 (2C), 127.9 (2C), 127.5 (2C), 121.5, 69.0, 68.4, 52.7, 50.6, 39.4, 29.0, 28.8, 27.0, 25.2, 23.5, 21.5, 21.2, 13.7, 13.0, 12.4.; HRMS (ESI-TOF, HCO_2Na): MNa^+, found 654.1666. $C_{30}H_{41}NNaO_4S^{120}Sn$ requires 654.1676.

*4.3.10. (2S,3S)-Methyl 3-allyl-2-(p-tolyl)-5-methylene-1-tosylpiperidine-3-carboxylate (**4e**).* Colorless solid; mp 154.0–155.0 °C; $[\alpha]_D$ +4.7 (*c* 0.21, $CHCl_3$); ν_{max} (neat) 1737, 1365, 1354, 1228, 1217, 1205 cm^{-1}; δ_H (500 MHz $CDCl_3$) 7.20 (d, *J*=8.0 Hz, 2H), 7.05 (d, *J*=7.3 Hz, 2H), 6.95 (d, *J*=8.2 Hz, 2H), 6.89 (d, *J*=7.7 Hz, 2H), 5.55 (dddd, *J*=19.2, 10.6, 6.2, 1.6 Hz, 1H), 5.16 (s, 1H), 5.11–5.01 (m, 3H), 4.94 (s, 1H), 4.25 (dd, *J*=13.7, 2.0 Hz, 1H), 3.73 (d, *J*=13.3 Hz, 1H), 3.40 (s, 3H), 2.90 (d, *J*=14.8 Hz, 1H), 2.68 (dd, *J*=13.8, 7.9 Hz, 1H), 2.58 (dd, *J*=14.6, 6.4 Hz, 1H), 2.47 (d, *J*=15.6 Hz, 1H), 2.29 (s, 3H), 2.25 (s, 3H).; δ_C (126 MHz, $CDCl_3$) 173.2, 142.7, 137.7, 137.1, 135.9, 134.1, 132.6, 129.1 (2C), 128.9 (2C), 128.8 (2C), 127.2 (2C), 119.3, 114.5, 62.7, 51.7, 51.2, 47.5, 39.8, 31.3, 21.5, 21.0.; HRMS (ESI-TOF, HCO_2Na): MNa^+, found 462.1713. $C_{25}H_{29}NNaO_4S$ requires 462.1715.

Supplementary data

Supplementary data (Spectroscopic charts for compounds **2** and **4**.) associated with this article can be found in the online version, at http://dx.doi.org/10.1016/j.tet.2016.04.078.

References and notes

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12. If an equilibrium process dominates in the formation of intermediate radical **F**, *Z*-configuration in intermediated **C** should be much preferred because of avoiding steric hindrance caused between they methylene radical and the Bu_3Sn group in **C**. However, *E*-**C** intermediate is mainly formed in the reaction performed at lower temperature (Scheme 5). In addition, we observed tin radical always attacks the alkene unit first to form intermediate **B** in the previous results. See refs. 5 and 6.
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