

Regio- and Stereoselective Synthesis of Allylic and Homoallylic Alcohols
by the Reductive Desulfonylation of Allylic Sulfone Derivatives.
Application to the Syntheses of (±)-Lavandulol and Isolavandulol[#]

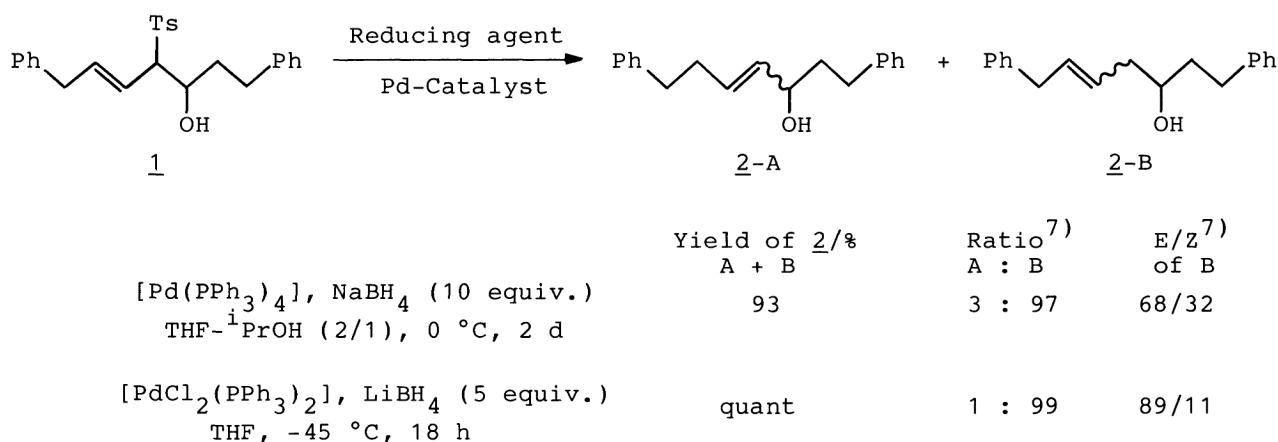
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Regio- and stereoselective desulfonylation of β-tosylhomoallylic alcohols provided a convenient method for the preparation of allylic and homoallylic alcohols. (±)-Lavandulol and isolavandulol were synthesized in excellent yields by this method.

Allylic sulfones are useful synthetic intermediates¹⁾ because of the ability of the sulfonyl group to generate an adjacent carbanion²⁾ and to act as a leaving group in substitution³⁾ and elimination⁴⁾ reactions. As a part of our investigation on the syntheses^{5a-c)} and reactions^{6a-e)} of allylic sulfones, we previously reported the regio- and stereoselective synthesis of homoallylic alcohols and terpenoids by the reductive desulfonylation of allylic sulfone derivatives with the combination of (1) NaBH₄/a catalytic amount of [Pd(PPh₃)₄]^{6a)} and (2) LiHBET₃/a catalytic amount of [PdCl₂(dppp)],^{6c,e)} respectively. We herein report a convenient method for the preparation of allylic and homoallylic alcohols by the regio- and stereoselective desulfonylation of the allylic sulfone derivatives.

The combination of NaBH₄ and a catalytic amount of [Pd(PPh₃)₄] was first employed for the desulfonylation of (E)-1,7-diphenyl-4-tosyl-5-penten-3-ol (1, mixture of 38/62 of diastereoisomers). The total yield of the reduction products

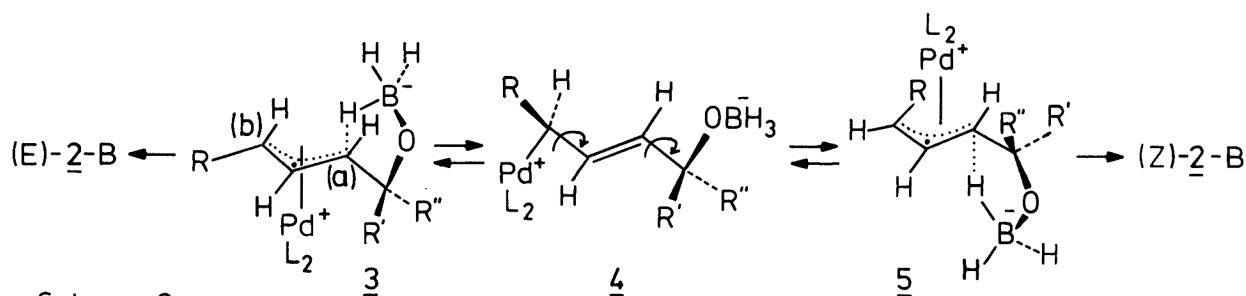


Scheme 1. Palladium-catalyzed desulfonylation of allylic sulfone derivative (1).

[#] Dedicated to Professor Teruaki Mukaiyama on the occasion of his 60th birthday.

(2-A,B) was excellent as expected, however, the partial migration of the double bond (2-A) and the formation of a geometrical isomer ((Z)-2-B) were observed as shown in Scheme 1 in contrast with the cases examined previously,^{6a)} in which the double bond was either stabilized by conjugation with a phenyl group or disubstituted with methyl groups, or else it was a terminal olefin. In order to overcome such problems, various conditions (catalyst:⁸⁾ $[\text{Pd}(\text{PPh}_3)_4]$ and $[\text{PdCl}_2\text{L}_2]$ (L: PPh_3 , $\text{P}(\text{OPh})_3$, PhCN ; L_2 : dppe, dppp, dppb, dppf); reducing agent: NaBH_4 , LiBH_4 , and LiAlH_4 ; solvent: THF-ROH, EtOH, and THF; reaction temperature: -45°C - 0°C) were reinvestigated. It was consequently found that (1) $[\text{PdCl}_2(\text{PPh}_3)_2]$ was the best catalyst, (2) LiBH_4 was better than NaBH_4 and LiAlH_4 , and (3) lower temperature was favorable to result in high regio- and stereoselectivity, though the reaction was retarded. The best conditions were shown in Scheme 1.

The desulfonylation seemed to proceed through an intermediary π -allyl complex (3 in Scheme 2), in which the position (a) is selectively reduced via a five-membered cyclic transition state. The formation of the (Z)-isomer suggests the existence of an equilibrium between the π -allyl complexes 3 and 5 through the σ -complex 4, probably due to the steric interaction between the palladium and/or its ligands and the substituent R' especially when R' is more bulky than R'' .



Scheme 2.

We next tried to prepare allylic alcohols by the reductive desulfonylation of the similar allylic sulfone derivatives such as 6. Namely, if the hydroxyl group is protected with a bulky group to prevent the intra- and/or intermolecular reduction on position (a) of the intermediate 3 in Scheme 2, the allylic alcohols seem to be formed by the selective reduction on the position (b) probably using a bulky reducing agent. From the results of a lot of experiments, the combination of $[\text{PdCl}_2(\text{dppb})]$ and LiHBET_3 proved to be the best for this purpose. Table 1 shows the influence of additives on such reductive desulfonylation of 6. As can be seen in the Table, tributyltin chloride (Entry 2), tributyltin hydride (6), triethyl- or triphenylsilyl hydride (8,9), and triphenylsilyl chloride (10) were so effective as additives that the reduction proceeded readily and selectively. It is noteworthy that the real reductant was not trisubstituted tin or silyl hydride (Entries 5 and 7) in the present reaction, in contrast to the reported ones,⁹⁾ but LiHBET_3 itself. From the fact that the reaction was rather retarded when a catalytic amount of tributyltin chloride or hydride was added (Entries 2 and 6) in spite of the improvement of the regioselectivity, compared to the case of the absence of an additive (Entry 1), the trisubstituted tin group (and probably silyl group too) seems to be bound to or exist around palladium ion of the catalyst.¹⁰⁾

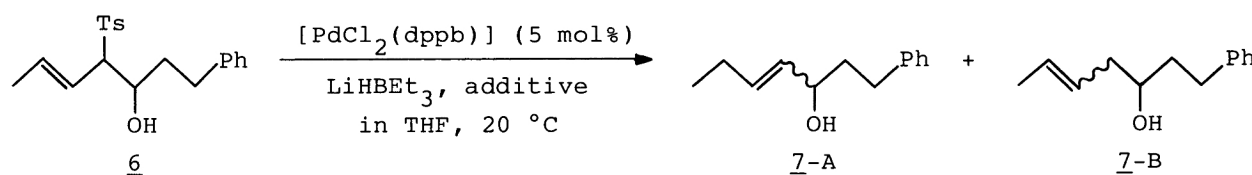
From the effectiveness and the easiness to handle, triphenylsilyl hydride was

preferred as an additive to prepare the allylic alcohols by the reductive desulfonylation of allylic sulfone derivatives.

Now it has become possible to prepare allylic and homoallylic alcohols selectively from the same allylic sulfone derivatives, β -tosylhomoallylic alcohols, by the reductive desulfonylation as listed in Table 2. Such reductive systems were successfully employed in the syntheses of (+)-lavandulol (13-B)¹¹⁾ and Isolavandulol (13-A)¹¹⁾ as shown in Scheme 3.

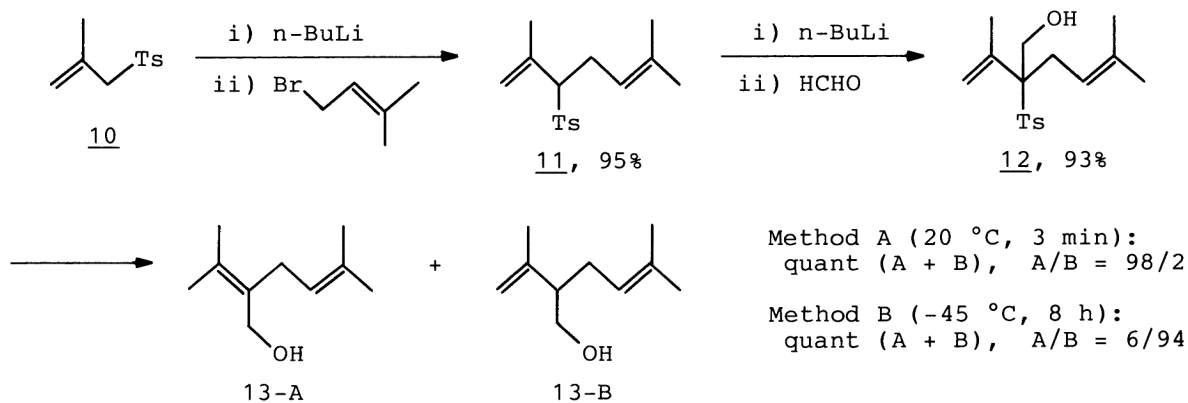
Further work is in progress to elucidate the scope and limitation of the present reduction systems in our laboratory.

Table 1. The Influence of Additives on the Reductive Desulfonylation of 6



Entry	Additive (equiv.)	LiHBET ₃ equiv.	Time	Yield of A + B	Ratio ^{a)} A : B	E/Z ^{a)} of A
1	—	3	3 min	95	87 : 13	96/4
2	n-Bu ₃ SnCl (0.2)	3	15 min	96	95 : 5	97/3
3	Me ₃ SnCl (0.2)	3	overnight	trace	94 : 6	97/3
4	Ph ₃ SnCl (0.2)	3	overnight	—	—	—
5	n-Bu ₃ SnH (3.0)	—	2 d	—	—	—
6	n-Bu ₃ SnH (0.2)	3	30 min	99	92 : 8	96/4
7	Et ₃ SiH (3.0)	—	5 h	—	—	—
8	Et ₃ SiH (0.2)	3	3 min	quant	97 : 3	98/2
9	Ph ₃ SiH (0.2)	3	3 min	quant	98 : 2	98/2
10	Ph ₃ SiCl (0.2)	3	3 min	98	96 : 4	98/2

a) Determined by 400 MHz ¹H-NMR spectra.



Scheme 3. Regio- and stereoselective synthesis of isolavandulol (13-A) and (+)-lavandulol (13-B) via same intermediate (12).

Table 2. Regio- and Stereoselective Synthesis of Allylic (A) and Homoallylic (B) Alcohols by the Reductive Desulfonylation of Allylic Sulfone Derivatives

(<u>8a-g</u>) ^{a)}	R ¹	Substrates R ²	Methods ^{b)}	Conditions	Yield of A + B	Ratio ^{c)} A : B	E/Z ^{c)} of main product
<u>8a</u>	CH ₃	PhCH ₂ CH ₂	A B	20 °C, 3 min -15 °C, 4.5 h	quant quant	98 : 2 3 : 97	98/2 91/9
<u>8b</u>	CH ₃	CH ₃ (CH ₂) ₇	A B	20 °C, 20 min -18 °C, 4 h	98 96	92 : 8 3 : 97	98/2 90/10
<u>8c</u>	PhCH ₂	CH ₃	A B	20 °C, 3 min -4 °C, 2.5 h	quant quant	93 : 7 7 : 93	96/4 89/11
<u>8d</u>	PhCH ₂	CH ₃ (CH ₂) ₇	A B	20 °C, 3 min -5 °C, 3 h	92 83	99 : 1 1 : 99	98/2 86/14
<u>8e</u>	PhCH ₂	(CH ₃) ₂ CH	A B	20 °C, 15 min 0 °C, 4 h	78 98	98 : 2 16 : 84	96/4 76/24
<u>8f</u>	PhCH ₂	PhCH ₂ CH ₂	A B	20 °C, 3 min -45 °C, 18 h	94 quant	96 : 4 1 : 99	96/4 89/11
<u>8g</u>	(CH ₃) ₂ CH	PhCH ₂ CH ₂	A B	20 °C, 45 min -20 °C, 7 h	99 87	93 : 7 3 : 97	98/2 >99/-

a) 8a = 6, 8f = 1; These were mixtures of diastereoisomers. Their ratios are given in the following: 8a (42/58), 8b (52/48), 8c (51/49), 8d (39/61), 8e (35/65), 8f (38/62), 8g (42/58). b) Method A: [PdCl₂(dppb)] (5 mol%), Ph₃SiH (0.2 equiv.), LiHBet₃ (3 equiv.) in THF; Method B: [PdCl₂(PPh₃)₂] (5 mol%), LiBH₄ (5 equiv.) in THF. c) Determined by 400 MHz ¹H-NMR spectra.

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- 7) Determined by 400 MHz ¹H-NMR spectra.
- 8) Five mol% of the catalyst was used in each case. dppe, dppp, dppb, and dppf mean 1,3-bis(diphenylphosphino)ethane, -propane, -butane, and 1,1'-bis(diphenylphosphino)ferrocene, respectively.
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