CHEMISTRY LETTERS, pp. 451 - 454, 1985.

PALLADIUM-CATALYZED REGIO- AND STEREOSELECTIVE DESULFONYLATION OF ALLYLIC SULFONES WITH LiHBEt$_3$.

APPLICATION TO THE SYNTHESIS OF SQUALENE

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Allylic p-tolyl sulfones were easily desulfonylated to the corresponding alkenes by LiHBEt$_3$ in the presence of a catalytic amount of [PdCl$_2$(dppp)] under mild conditions with the preservation of the original stereochemistry. This reaction was successfully applied to the synthesis of squalene.

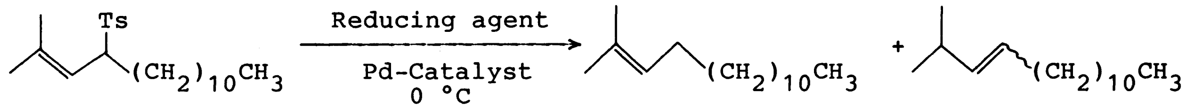
We previously reported the regioselective synthesis of homoallylic alcohols by reductive desulfonylation of allylic sulfone derivatives with sodium borohydride using [Pd(PPh$_3$)$_4$] as a catalyst.$^{1)}$ It was applied to the other allylic sulfones such as 2-methyl-4-(tolylsulfonyl)-2-pentadecene (1), however, the expected product (2a) could not be obtained as seen in Table 1 (Entry 1). As shown in Entries 2 and 3, the use of Pd(II) complexes as a catalyst gave better results than Pd(0) complex.

On the other hand, R. O. Hutchins and K. Learn have reported that the combination of [Pd(PPh$_3$)$_4$] and LiHBEt$_3$ provided an effective system for reductive removal of allylic functional groups including allylic sulfones.$^{2)}$ The combination of Pd(II) complex and LiHBEt$_3$ was therefore examined. It was found that [PdCl$_2$(dppp)] was the best catalyst (see Entry 7) among the examined ones in both respects of reactivity and regioselectivity.

The present reductive desulfonylation using [PdCl$_2$(dppp)] as a catalyst was applied to a variety of allylic sulfones listed in Table 2. The regio- and stereoselectivity are excellent and the yields of the products are high.

The experimental procedure is described for the reduction of 1: To a solution of 1 (57 mg, 0.15 mmol) and 5 mol% of [PdCl$_2$(dppp)] (3.6 mg) in THF (4 ml) was

Table 1. Palladium-Catalyzed Desulfonylation of Allylic Sulfone (1) under Various Conditions

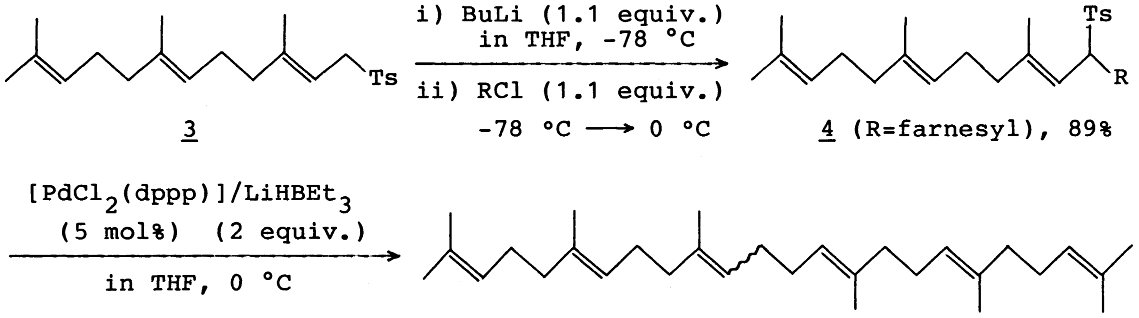


1 2a 2b

Entry	Pd-Catalyst[a]	Reducing agent	Time / h	Solvent	Isolated yield/%	Recovery of 1/%	Ratio[b] a : b
1	$[Pd(PPh_3)_4]$	$NaBH_4$	11	THF-EtOH (1 : 7)	0	quant	-
2	$[PdCl_2(PPh_3)_2]$	$NaBH_4$	43	DMF-HMPA-H_2O (200:100:1)	24	58	74 : 26
3	$[PdCl_2(dppp)]$	$NaBH_4$	43	DMF-HMPA-H_2O (200:100:1)	33	65	80 : 20
4	$[Pd(PPh_3)_4]$	$LiHBEt_3$	5	THF	<5	95	67 : 33
5	$[PdCl_2(PPh_3)_2]$	$LiHBEt_3$	5	THF	<3	96	49 : 51
6	$[PdCl_2(dppe)]$	$LiHBEt_3$	5	THF	33	58	97 : 3
7	$[PdCl_2(dppp)]$	$LiHBEt_3$	1.5	THF	86	-	>99 : -

a) 5 mol% of the catalyst was used in each case. dppe and dppp mean 1,2-bis(diphenylphosphino)ethane and 1,3-bis(diphenylphosphino)propane, respectively.
b) Determined by GLPC analyses.

added 0.3 ml (0.3 mmol) of 1 M THF solution of $LiHBEt_3$ at 0 °C under nitrogen. After stirring for 1.5 h at 0 °C, the reaction mixture was treated with 3 M NaOH (1 ml) and a small amount of aqueous KCN solution with stirring for 30 min followed by addition of NaCl and extraction with hexane. The residue obtained by evaporation of the solvent was separated with a preparative TLC (SiO_2, hexane) to afford 2-methyl-2-pentadecene (2a, 29 mg) in 86% yield.



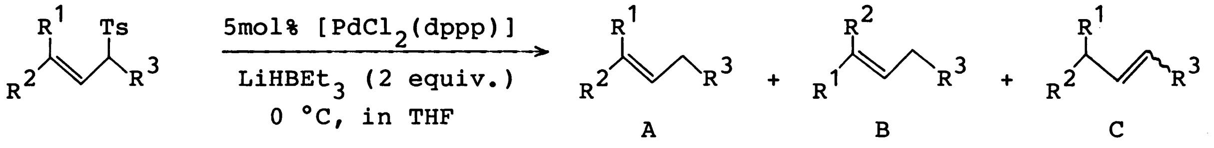
3

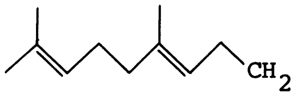
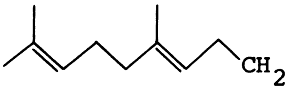
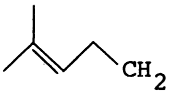
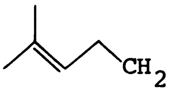
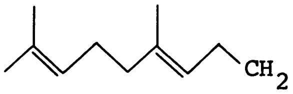
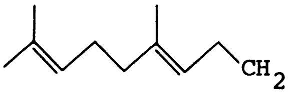
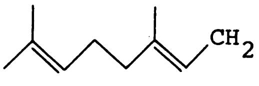
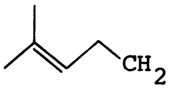
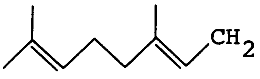
4 (R=farnesyl), 89%

E (5a), Z (5b)
total yield 94% (5a : 5b = 97 : 3)

Scheme 1. Synthesis of Squalene.

Table 2. Palladium-Catalyzed Desulfonylation of Allylic Sulfones with $LiHBEt_3$



Substrate R^1	R^2	R^3	Reaction time	Isolated yield/%[a]	Ratio[b] A : B : C
CH_3		H	30 min	87	97 : 2 : 1
	CH_3	H	40 min	91	88 : 11 : 1
CH_3	CH_3	$CH_3(CH_2)_{10}$	1.5 h	86	>99 : - : -
CH_3		$CH_3(CH_2)_{10}$	1.5 h	98	94 : 6 : -
	CH_3	$CH_3(CH_2)_{10}$	5 h	83	91 : 9 : -
CH_3		$CH_3(CH_2)_{10}$	4.5 h	82	92 : 7 : 1
	CH_3	$CH_3(CH_2)_{10}$	4 h	77	95 : 5 : -
H	C_6H_5	$CH_3(CH_2)_{10}$	40 min	quant	84 : - : 16
H	C_6H_5	$C_6H_5CH_2$	30 min	94	94 : - : 6
CH_3	CH_3		30 min	91	>99 : - : -
CH_3			1 h	92	98 : 2 : -

a) Separated with a preparative TLC (silica gel). All products exhibited satisfactory spectral data.

b) Determined by GLPC analyses and 400 MHz ^{1}H-NMR spectra.

The present desulfonylation was successfully employed in the synthesis of squalene (5a) starting from farnesyl p-tolyl sulfone (3) which is readily prepared by our method,[3)] in two steps as outlined in Scheme 1.

Further work is in progress to elucidate the scope and limitation[4)] in our laboratory.

We are grateful to Dr. Yoshiji FUJITA, Central research Lab., Kuraray Co. Ltd., for gifts of (E)-geraniol and (E,E)-farnesol.

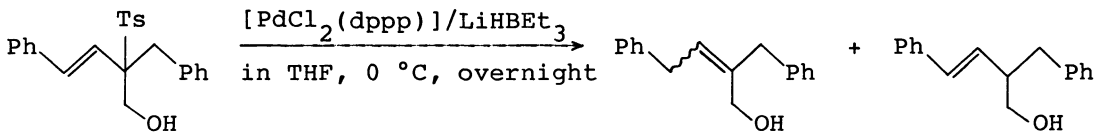
References

1) H. Kotake, T. Yamamoto, and H. Kinoshita, Chem. Lett., 1982, 1331.

2) R. O. Hutchins and K. Learn, J. Org. Chem., 47, 4380 (1982).

3) K. Inomata, T. Yamamoto, and H. Kotake, Chem. Lett., 1981, 1357: When farnesyl acetate was treated with 1.1 equiv. of sodium p-toluenesulfinate tetrahydrate in the presence of 5 mol% of $[Pd(PPh_3)_4]$ in THF-MeOH (3 : 1, v/v) at room temperature overnight, 3 was obtained in 70% yield accompanied with 13% of its 2-Z isomer.

4) The migration of an olefinic double bond was observed when the present desulfonylation method was applied to 6 as shown in the following scheme, whereas the homoallylic alcohol (8) was exclusively formed by the previous method.[1)]



6 7, 71% (E/Z=84/16) 8, 5%

(Received January 5, 1985)