Stereochemistry of Palladium-catalyzed Asymmetric Transformation of Chiral 2-Alkynyl Sulfinates into Allenyl Sulfones

Kunio Hiroi,* Fumiko Kato, and Hajime Nakasato
Department of Synthetic Organic Chemistry, Tohoku College of Pharmacy, Sendai, Miyagi 981-8558

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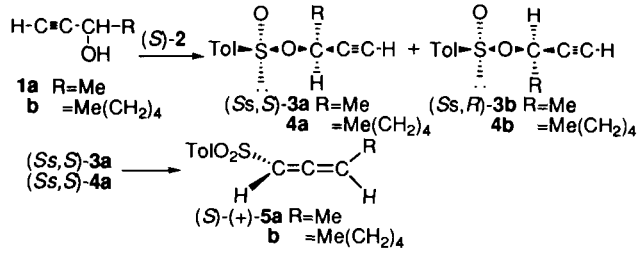
Optically active 2-alkynyl *p*-toluenesulfinates, possessing chirality on both the α-carbons of the 2-alkynyl groups and the sulfur atoms of the sulfinates, were readily transformed into chiral allenyl sulfones with high stereospecificity in good yields by treatment with palladium acetate. The stereochemistry of the transformation was determined and the plausible mechanistic pathway is proposed.

Axial chirality is one of the most interesting functionality for asymmetric induction and has received much attention in organic synthesis, especially for the application to asymmetric synthesis, in recent years.[1] We wish to demonstrate here the stereochemistry of the palladium-catalyzed transformation of chiral 2-alkynyl sulfinates, which have chirality on both the α-carbons of the 2-alkynyl groups and the sulfur atoms of the sulfinates, into chiral allenyl sulfones.[2] We wish also to represent a mechanistic pathway based on the rationalization of the stereochemical results obtained.

Chiral 2-alkynyl *p*-toluenesulfinates (*Ss*,*S*)-**3a** and **4a**, and (*Ss*,*R*)-**3b** and **4b** were readily obtained by $BF_3 \cdot OEt_2$-catalyzed alcoholysis of (*S*)-*N*,*N*-diethyl-*p*-toluenesulfinamide (**2**) with (±)-**1a,b** with 95 or 94% stereospecificity in 88% yield.[3] The absolute configuration of the sulfur atoms in **3a,b** and **4a,b** was determined as (*S*)-configuration.[3] The absolute configuration of the chiral carbon centers in **3a,b** and **4a,b** was determined by chemical correlation to 1-butyn-3-yl acetate[4a] and 1-octyn-3-ol[4b] of known absolute configuration.

Upon refluxing in chlorobenzene in the presence of lithium carbonate (0.5 equiv.) for 2-6 h, (*Ss*,*S*)-**3a** and **4a** and (*Ss*,*R*)-**3b** and **4b** underwent [2,3] sigmatropic rearrangements[5] to give chiral allenes (*S*)-(+)- and (*R*)-(-)-**5a,b** in almost quantitative yield, respectively.[6] The absolute configuration of the allenes **5a,b** was deduced on the basis of the most plausible mechanistic pathway *via* [2,3] sigmatropic rearragements.[5]



Scheme 1.

The palladium catalysis facilitates the transformation.[7] The chiral sulfinates (*Ss*,*S*)-**3a** and **4a** or (*Ss*,*R*)-**3b** and **4b** were treated with $Pd(OAc)_2$ (0.05 equiv.) in THF at room temperature in the presence of ligands (0.075 equiv.) to afford (*S*)-(+)-**5a,b** or (*R*)-(-)-**5a,b**, respectively. The e.e. of the product was determined by the HPLC analysis with chiralpack AD.

The stereospecificity of the reaction was calculated based on the optical purity of the starting sulfinate (87% e.e.) used and the allene obtained. The results obtained are summarized in Table 1. The rather unequivocal effects of phosphine ligands on the asymmetric induction were observed. Use of dpph as a ligand provided the highest stereospecificity.

Table 1. Palladium-Catalyzed Transformation of Chiral Sulfinates **3a,b** and **4a,b** into Chiral Allenes **5a,b**[a]

Sulfinate	Ligand[b]	Reaction time (h)	Isolated yield (%) of **5**	Stereospecificity (%) of **5**[c]
(*Ss*,*S*)-**3a**	dppe	18	65 (**5a**)	88 (*S*)
(*Ss*,*R*)-**3b**	dppe	18	75 (**5a**)	85 (*R*)
(*Ss*,*S*)-**3a**	dppb	18	72 (**5a**)	82 (*S*)
(*Ss*,*R*)-**3b**	dppb	18	80 (**5a**)	83 (*R*)
(*Ss*,*S*)-**3a**	dpph	18	74 (**5a**)	80 (*S*)
(*Ss*,*R*)-**3b**	dpph	18	89 (**5a**)	89 (*R*)
(*Ss*,*S*)-**3a**	PPh_3	16	65 (**5a**)	79 (*S*)
(*Ss*,*R*)-**3b**	PPh_3	16	64 (**5a**)	77 (*R*)
(*Ss*,*S*)-**4a**	dppb	28	46 (**5b**)	64 (*S*)
(*Ss*,*R*)-**4b**	dppb	18	50 (**5b**)	72 (*R*)
(*Ss*,*S*)-**4a**	dpph	24	39 (**5b**)	69 (*S*)
(*Ss*,*R*)-**4b**	dpph	24	51 (**5b**)	73 (*R*)
(*Ss*,*S*)-**4a**	PPh_3	24	53 (**5b**)	60 (*S*)
(*Ss*,*R*)-**4b**	PPh_3	24	61 (**5b**)	73 (*R*)

[a]The sulfinates (*Ss*,*S*)-**3a** and **4a** or (*Ss*,*R*)-**3b** and **4b** (87% e.e.) were treated with $Pd(OAc)_2$ (0.05 equiv.) in the presence of a phosphine ligand [0.075 equiv. except for PPh_3 (0.10 equiv.)] in THF at room temperature. [b]dppe: 1,2-bis(diphenylphosphino)ethane, dppb: 1,4-bis(diphenylphosphino)butane, dpph: 1,6-bis(diphenylphosphino)hexane. [c]The stereospecificity of the transformation was calculated by the e.e. of the starting sulfinates (87% e.e.) and the product **5** obtained by HPLC analysis with chiralpack AD.

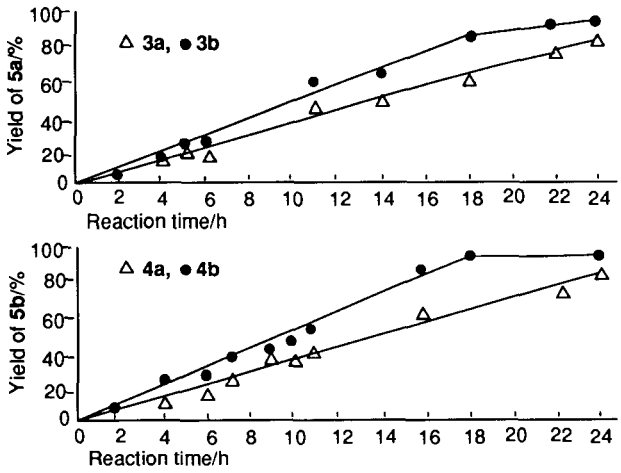
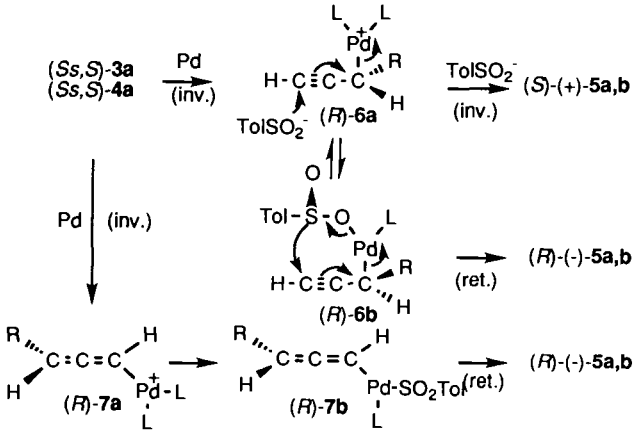


Figure 1. The conversion ratio of **3a,b** and **4a,b** into **5a,b**. Reaction conditions: $Pd(OAc)_2$, dppb, in THF, at 22 °C.

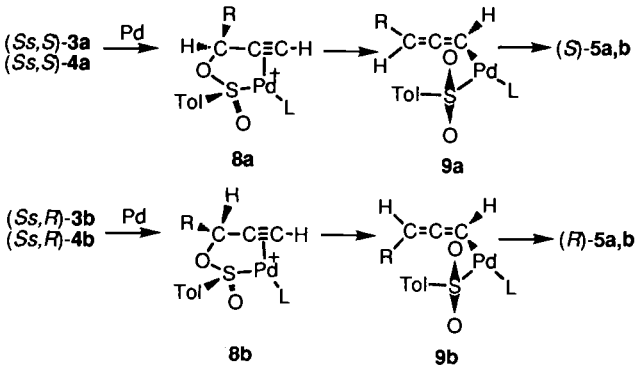
The yields of **5a,b** from (*Ss*,*S*)-**3a** and **4a** or (*Ss*,*R*)-**3b** and **4b** were plotted by the HPLC analysis with chiralpack AD in accordance with the elapse of the reaction time. The unequivocal difference of the conversion rate between the diastereoisomers was observed as shown in the Figure 1: the conversion rate of (*Ss*,*R*)-**3b** and **4b** was greater than that of the corresponding diastereoisomers (*Ss*,*S*)-**3a** and **4a**. The stereospecificity in the transformation of each diastereoisomer was not changeable with the elapse of the reaction time.

The plausible mechanism of this transfomation is presented as follows. The conjugate addition of a palladium catalyst to the γ-carbon of the 2-alkynyl group in (*Ss*,*S*)-**3a** and **4a** with inversion of configuration would give (*R*)-**7a**, followed by the sulfonylation with retention of configuration *via* (*R*)-**7b** to provide (*R*)-**5a,b**. This is not consistent with the result obtained. The substitution of the sulfinate with the palladium catalyst at the α-carbon of the 2-alkynyl group in (*Ss*,*S*)-**3a** and **4a** with inversion of configuration would afford (*R*)-**6a**. The intramolecular sulfonylation *via* (*R*)-**6b** with retention of configuration would give (*R*)-**5a,b**. However, this is not consistent with the experimental result. Therefore, it might be more reasonable that the sulfonylation of (*R*)-**6a** by conjugate addition of the *p*-toluenesulfonyl anion with inversion of configuration gives (*S*)-**5a,b**. However, if (*R*)-**6a** would be the most important key intermediate, each stereospecificity and chemical yield obtained from both the diastereoisomers should be almost the same. This reaction path to (*S*)-**5a,b** *via* (*R*)-**6a** would be rejected by the following result of the cross-sulfonylation reaction: the palladium-catalyzed reactions of (*Ss*,*S*)-**3a** and **4a** or (*Ss*,*R*)-**3b** and **4b** were carried out in the presence of sodium benzenesulfinate to give (*S*)- or (*R*)-**5a,b** respectively, without any formation of phenylsulfonyl allenes. This means the reactions would proceed, not *via* the ionic intermediate (*R*)-**6a**, through the intramolecular transformation mechanisms.



Scheme 2.

Thus, we wish to propose another novel mechanism *via* Pd(0)-mediated intermediates for this transformation by the direct participation of chirality of the sulfinate in the crucial stage of the transition states. The palladium-catalyzed reaction of (*Ss*,*S*)-**3a** and **4a** would be taken place by the initial formation of **8a** coordinated by the acetylene group and the sulfinate sulfur atom, which has rather potential ability of coordination to palladium. The allenylpalladium complex **9a** would be formed *via* **8a** with retention of configuration. The intramolecular sulfonylation of **9a** with retention of configuration would provide (*S*)-**5a,b**. Similarly, the palladium-catalyzed reaction of another diastereoisomer (*Ss*,*R*)-**3b** or **4b** would proceed *via* **8b** and **9b** to give (*R*)-**5a,b**. The afore-mentioned observation of the differences in the transformation rate between both the diastereoisomers (Figure 1) should be reasonably understandable. The transition state **8a** has steric hindrance between R and the tolyl group due to the *cis* configuration in the five-membered-like intermediate. Therefore, the reaction *via* **8a** could not be accessible with ease, and provided the rather low transformation rate, as shown in Figure 1, and the slightly low stereospecificity, presumably due to proceeding somewhat *via* the ionization mechanism, compared with those from **8b**.



Scheme 3.

Thus, the palladium-catalyzed reactions of the chiral sulfinates have been found very useful for providing optically active allenes. This is the first example of the synthesis of chiral allenes from propargylic alcohol derivatives bearing chiral leaving groups.

References and Notes

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6 The stereochemistry of these thermal rearrangements will be reported in due course.

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