Pergamon

Tetrahedron: *Asymmetry* 12 (2001) 37–40

TETRAHEDRON: *ASYMMETRY*

Stereochemistry of transition metal catalyzed asymmetric intramolecular allyl transfer in chiral α-sulfinyl allylic esters

Kunio Hiroi,* Yoshio Suzuki, Fumiko Kato and Yoshiko Kyo

Department of Synthetic Organic Chemistry, Tohoku Pharmaceutical University, 4-4-1 Komatsushima, Aoba-ku, Sendai, Miyagi 981-8558, Japan

Received 4 December 2000; accepted 11 January 2001

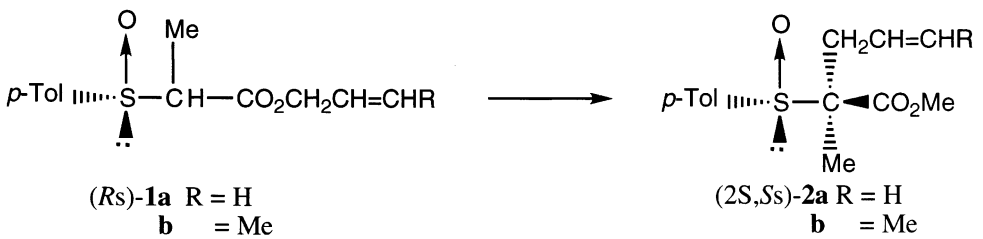
Abstract—The stereochemistry of palladium or nickel catalyzed asymmetric intramolecular allyl transfer in chiral α-sulfinyl allylic esters was determined. The participation of the catalyst and the chiral sulfinyl functionality in these transformations, presumably by the coordination of the sulfinyl group to the catalyst, is discussed, and a novel mechanism is proposed for the rationalization of the results obtained. © 2001 Elsevier Science Ltd. All rights reserved.

Transition metal catalyzed reactions have received much attention in recent years for achieving carbon–carbon bond forming reactions with high stereoselectivity, owing to the availability of milder reaction conditions with these catalysts.[1] Currently, we are developing a number of methods for asymmetric synthesis with transition metal catalysts,[2] especially those using a chiral organosulfur functionality.[3] Our recent research has been focused on the incorporation of a chiral sulfinyl moiety into transition metal catalysts. We wish to communicate herein our recent work concerning transition metal catalyzed intramolecular allyl transfer in chiral α-sulfinyl allylic esters, we propose a novel mechanism for allyl transfer in this system on the basis of our observations on the stereochemistry of the reactions.

Another interest focuses on two possible reaction paths in the transition metal catalyzed reactions of allylic esters, transition metal assisted [3,3]-sigmatropic rearrangements[4] and the intramolecular nucleophilic substitutions of π-allyl transition metal complexes.

Introduction of a chiral sulfinyl functionality into the reaction substrates and stereochemical studies with these substrates have enabled us to reveal the correct reaction path and the mechanism of asymmetric induction, particularly with respect to participation of the chiral sulfinyl groups in the transition metal catalysts.

Upon treatment with a palladium or nickel catalyst, the chiral 2-(*p*-toluenesulfinyl)propionic allylic esters (*R*s)-**1a** and **1b**, underwent asymmetric intramolecular allyl transfer reactions to give α-allylic propionic esters with high diastereoselectivity. After chiral α-sulfinyl propionic allyl ester (*Rs*)-**1a** was treated with *sec*-butyllithium or lithium diisopropylamide (LDA) (1.0 equiv.), the reactions of the lithium enolate generated were carried out in THF in the presence of $Pd(PPh_3)_4$ (0.1 equiv.) and PPh_3 (0.2 equiv.), followed by treatment



(*R*s)-**1a** R = H
b = Me

(2S,*S*s)-**2a** R = H
b = Me

Scheme 1.

* Corresponding author. E-mail: khiroi@tohoku-pharm.ac.jp

PII: S0957-4166(01)00030-1

with (trimethylsilyl)diazomethane, to give (2*S*,*S*s)-**2a** (Scheme 1) with very high diastereoselectivity (85–94%), as listed in Table 1.

The palladium catalyzed reactions of the lithium enolate of the chiral α-sulfinyl propionic crotyl ester (*R*s)-**1b** (generated by treating with *sec*-butyllithium or LDA) were carried out in THF at −20°C to furnish exclusively (2*S*,*S*s)-**2b** with good diastereoselectivity of 79%. On raising the reaction temperature to 0°C, an excellent d.e. of 98–99% was observed. Both reactions proceeded without formation of the [3,3]-sigmatropic rearrangement product, methyl 2,3-dimethyl-2-(*p*-toluenesulfinyl)-4-pentenoate.

It should be noted, however, that the nickel catalyzed reaction of the lithium enolate of (*R*s)-**1a** gave an allylated product with the same absolute configuration to that obtained by a similar palladium catalyzed reaction; the reaction of (*R*s)-**1a** was carried out in THF at room temperature in the presence of bis(cyclooctadienyl)nickel [$Ni(COD)_2$] (0.1 equiv.) and PPh_3 (0.2 equiv.), followed by treatment with (trimethylsilyl)diazomethane, to afford (2*S*,*S*s)-**2a** in 18% yield with high 87% diastereoselectivity.

The diastereomeric excess (d.e.) of the products was calculated by HPLC analysis with ODS. The results obtained are summarized in Table 1.

For comparison, intermolecular asymmetric allylations of methyl (*R*s)-2-(*p*-toluenesulfinyl)propionate **3** with or without a palladium catalyst were studied. The lithium enolate of (*R*s)-**3** (generated by treating with *sec*-butyllithium) was reacted with allyl acetate (2.0 equiv.) in THF at room temperature, 0 and −20°C in the presence of $Pd(PPh_3)_4$ (0.2 equiv.) and PPh_3 (0.4 equiv.) to afford (2*S*,*S*s)-**2a** with 4% d.e. obtained at room temperature. The d.e. increased to 37% in the 0°C reaction, and unexpectedly (2*R*,*S*s)-**2a** was formed at −20°C with 15% d.e. The reaction at −78°C provided no allylated product.

The allylation reaction of (*R*s)-**3** with allyl bromide (1.5 equiv.) in THF at 0°C in the absence of a palladium catalyst gave the unexpected (2*R*,*S*s)-**2a** in 57% yield

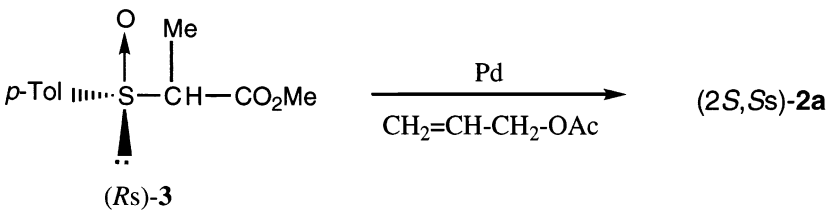
Table 1. Transition metal catalyzed asymmetric intramolecular allyl transfer in chiral α-sulfinyl allylic esters (*R*s)-**1a**,**b**[a]

	Base	Reaction temp. (°C)	Yield (%) of (2*S*,*S*s)-**2a**,**b**	D.e. (%) of (2*S*,*S*s)-**2a**,**b**[b]
(*R*s)-**1a**	*sec*-BuLi	0	40	85
	sec-BuLi	−20	32	94
	LDA	0	54	94
	sec-BuLi	Rt	18[c]	87
(*R*s)-**1b**	*sec*-BuLi	−20	31	79
	sec-BuLi	0	73	98
	LDA	0	32	99

[a] The reactions of (*R*s)-**1a**,**b** were carried out in THF for 12 h in the presence of $Pd(PPh_3)_4$ (0.1 equiv.) and PPh_3 (0.2 equiv.), followed by treatment with (trimethylsilyl)diazomethane.

[b] The diastereomeric excess (d.e.) of (2*S*,*S*s)-**2a**,**b** was calculated by HPLC analysis with ODS.

[c] The reaction of (*R*s)-**1a** was carried out in THF for 12 h in the presence of $Ni(COD)_2$ (0.1 equiv.) and PPh_3 (0.2 equiv.), followed by treatment with (trimethylsilyl)diazomethane.



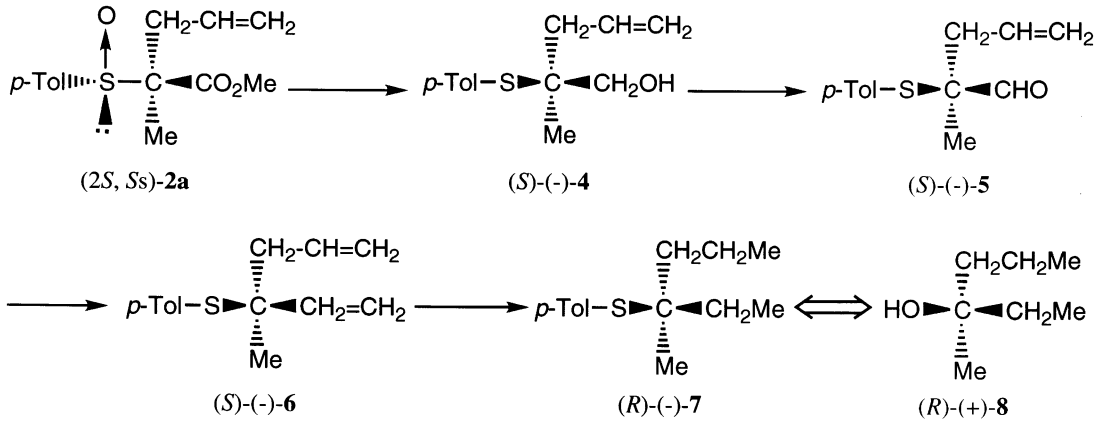
Scheme 2.

Table 2. Palladium catalyzed intermolecular asymmetric allylations of (*R*s)-**3**[a]

Reaction temp. (°C)	Reaction time (h)	Yield (%) of (*S*s)-**2a**	D.e. (%) of (*S*s)-**2a**
Rt	6	38	4 (2*S*)
0	7	49	37 (2*S*)
−20	17	28	15 (2*R*)
−78	12	–	–
0	17	57[b]	39 (2*R*)

[a] The lithium enolate, generated from (*R*s)-**3** and *sec*-BuLi (1.2 equiv.), reacted with allyl acetate (2.0 equiv.) in THF in the presence of $Pd(PPh_3)_4$ (0.2 equiv.) and PPh_3 (0.4 equiv.).

[b] The reaction of the lithium enolate of (*R*s)-**3** with allyl bromide (1.5 equiv.) was carried out in THF without the palladium catalyst.



Scheme 3.

with 39% diastereoselectivity (Scheme 2). The results obtained are summarized in Table 2.

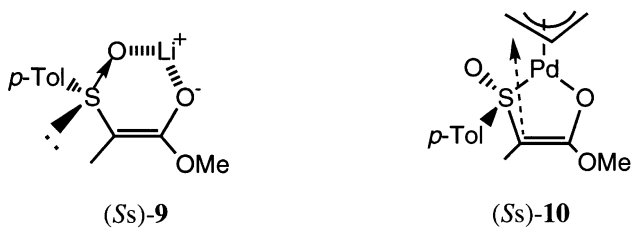
The absolute configuration of the product, **2a**, was determined by chemical correlation to 3-methyl-3-hexen-2-ol **8** of known absolute configuration[5] as follows. The product (2*S*,*S*s)-**2a** obtained by the palladium catalyzed reaction of (*Ss*)-**1a** was reduced with $LiAlH_4$ to give alcohol (*S*)-(−)-**4**, oxidation with CrO_3–pyridine, followed by condensation of the aldehyde (*S*)-(−)-**5** obtained with triphenylphosphine methylide in a Wittig reaction gave (*S*)-(−)-**6**. Reduction of the olefin (*S*)-(−)-**6** with diimide afforded sulfide (*R*)-(−)-**7**, which was chemically correlated to (*R*)-(+)-**8** of known absolute configuration[5] by nucleophilic substitution of a mesylate of (*R*)-(+)-**8** with sodium *p*-toluenethiolate, which occurred with inversion of configuration to yield (*S*)-(+)-**7** (Scheme 3).

The results obtained can be rationalized by the following mechanism: the intermolecular allylation of (*R*s)-**3** with allyl bromide at 0°C in THF using LDA as a base would proceed via a lithium chelate of the enolate (*S*s)-**9** coordinated by the sulfinyl oxygen atoms, the formation of chelates of lithium or magnesium enolates with sulfinyl oxygen atoms has precedence from many investigators.[6] Allyl bromide attacks from the less crowded lone pair side of the sulfinyl group to give (2*R*,*S*s)-**2a** in 57% yield with 39% d.e. The palladium catalyzed allylation of the enolate of (*R*s)-**3** with allyl acetate would proceed via a different reaction path; at −20°C, the reaction would occur via (*S*s)-**9** in a similar way to the reaction with allyl bromide, giving (2*R*,*S*s)-**2a** with low d.e. of 15%, whereas the allylation reaction at higher temperatures (0°C or room temperature) would proceed via the palladium chelate **10** (Scheme 4) obtained by transmetallation of the lithium enolate with a palladium catalyst and coordination of a chiral sulfinyl sulfur atom,[3e] presumably by intramolecular or intermolecular allylation with a π-allyl-palladium complex as an allylating reagent from the sterically less crowded (sulfinyl oxygen downward) side, giving (2*S*,*S*s)-**2a** in 38 or 49% yield with 4 or 37% d.e., respectively.

On the basis of the above-mentioned rationalization of the intermolecular allylation, the intramolecular palladium catalyzed reaction is elucidated as follows. There are two possible reaction paths in palladium catalyzed reactions of allylic ester enolates as mentioned before (no thermal [3,3]-sigmatropic rearrangement occurred under the mild reaction conditions employed in these models). It should certainly be concluded that allylic ester enolates undergo intramolecular allylation of ester enolates via π-allyl-metal complexes, upon treatment with a palladium or nickel catalyst, since the palladium catalyzed reaction of the lithium enolate of (*S*s)-**1b** provided exclusively **2b** without any formation of the Claisen rearrangement product.

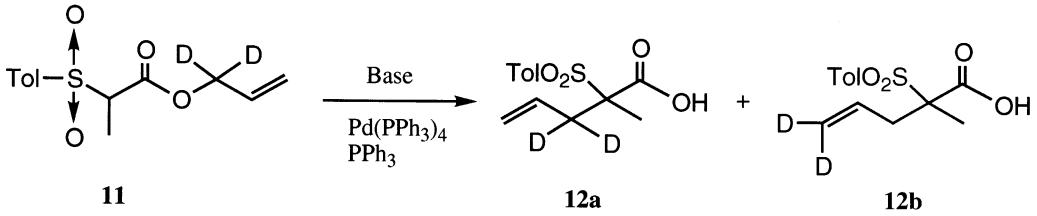
Further studies using a reaction substrate incorporating deuterium atoms reveal that the most plausible reaction path should be a course via π-allyl metal complexes, not by [3,3]-sigmatropic rearrangements; the palladium catalyzed reactions of 1,1-dideuterioallyl 2-*p*-toluenesulfonylpropionate **11** provided a 1:1 mixture of 3,3- or 5,5-dideuterio-2-methyl-2-(*p*-toluenesulfonyl)-4-pentenoic acids **12a** and **12b** (Scheme 5).

Thus, as designated in Scheme 6, the intramolecular allylation via (*S*s)-**13a** from the sterically less crowded sulfinyl sulfur lone pair side provides (2*R*,*S*s)-**2a**. However, the explanation via a path involving (*S*s)-**13a** is in conflict with the experimental result. Therefore, it should be certainly assumed that the reaction proceeds via a palladium chelate (*S*s)-**13c**, obtained through equilibrium via an enolate (*S*s)-**13b**, coordinated by a chiral sulfinyl sulfur atom.[3e] Here, the allylation would occur from the less sterically crowded (sulfinyl oxygen

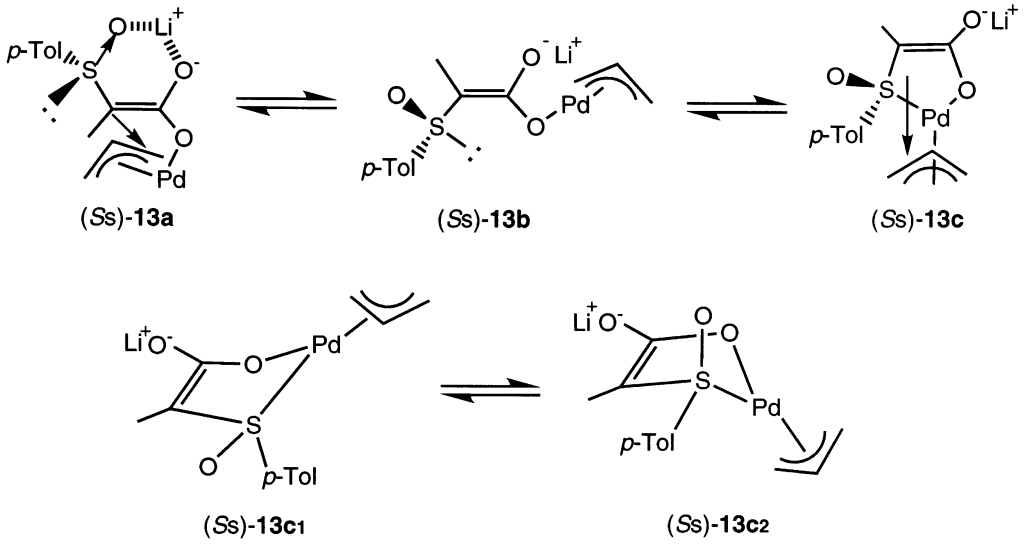


(*S*s)-**9** (*S*s)-**10**

Scheme 4.



Scheme 5.



Scheme 6.

upward) side of the preferred conformer (*S*s)-**13c1** in the conformational equilibrium of the five-membered palladium complex, providing (2*S*,*S*s)-**2a**.

Extremely high enantioselectivity was observed in transition metal catalyzed asymmetric intramolecular allyl transfer of chiral α-sulfinyl allylic esters. A novel mechanism is assumed for rationalization of the stereochemical outcome obtained.

References

1. (a) Brunner, H. *Synthesis* **1988**, 645–654; (b) Blystone, S. L. *Chem. Rev.* **1989**, 1663–1679; (c) Ojima, I.; Clos, N.; Bastos, C. *Tetrahedron* **1989**, *45*, 6901–6939; (d) Sawamura, M.; Ito, Y. *Chem. Rev.* **1992**, *92*, 857–871.
2. (a) Hiroi, K.; Abe, J.; Suya, K.; Sato, S.; Koyama, T. *J. Org. Chem.* **1994**, *59*, 203–213 and references cited therein; (b) Hiroi, K.; Kato, F.; Yamagata, A. *Chem. Lett.* **1998**, 397–398.
3. (a) Hiroi, K.; Arinaga, Y. *Tetrahedron Lett.* **1994**, *35*, 153–156; (b) Hiroi, K.; Kato, F.; Nakasato, H. *Chem. Lett.* **1998**, 553–554; (c) Hiroi, K.; Suzuki, Y. *Tetrahedron Lett.* **1998**, *39*, 6499–6502; (d) Hiroi, K.; Suzuki, Y.; Abe, I.; Hasegawa, Y.; Suzuki, K. *Tetrahedron: Asymmetry* **1998**, *9*, 3797–3817; (e) Hiroi, K.; Suzuki, Y.; Kawagishi, R. *Tetrahedron Lett.* **1999**, *40*, 715–718; (f) Hiroi, K.; Yoshida, Y.; Kaneko, Y. *Tetrahedron Lett.* **1999**, *40*, 3431–3434; (g) Hiroi, K.; Suzuki, Y.; Abe, I.; Kawagishi, R. *Tetrahedron* **2000**, *56*, 4701–4710.
4. Tsuji, J. *Palladium Reagents and Catalysts*; John Wiley & Sons: Chichester, 1995; pp. 400–404 and references cited therein.
5. Kirmse, W.; Knist, J.; Ratajczak, H.-J. *Chem. Ber.* **1976**, *109*, 2296–2314.
6. (a) Kunieda, N.; Nokami, J.; Kinoshita, M. *Chem. Lett.* **1974**, 369–372; (b) Mioskowski, C.; Solladie, G. *J. Chem. Soc., Chem. Commun.* **1977**, 162–163; (c) Mioskowski, C.; Solladie, G. *Tetrahedron* **1980**, *36*, 227–236; (d) Posner, G. H.; Mallamo, J. P.; Miura, K. *J. Am. Chem. Soc.* **1981**, *103*, 2886–2887; (e) Solladie, G.; Matloubi-Mogadham, F. *J. Org. Chem.* **1982**, *47*, 91–94.