[Chem. Pharm. Bull. 36(5)1744—1749(1988)]

Asymmetric Induction Reactions. III. Palladium-Catalyzed Asymmetric Sulfonylations of Allylic Sulfinates and Acetates with Chiral Phosphine Ligands

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(Received October 29, 1987)

Treatment of allylic (±)-*p*-toluenesulfinate with tetrakis(triphenylphosphine)palladium in the presence of chiral phosphine ligands resulted in allylic sulfinate–sulfone rearrangements to give the corresponding optically active allylic sulfones in high optical yields. The palldium-catalyzed reactions of readily obtainable allylic acetates with sodium *p*-toluenesulfinate in the presence of chiral phosphine ligands provide a new method for preparation of optically active allylic sulfones with high enantiomeric excess.

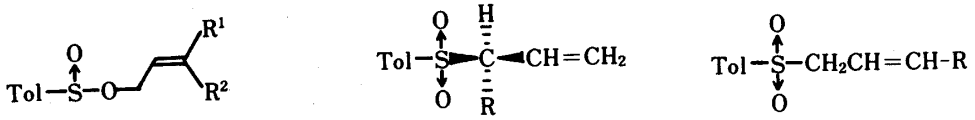
Keywords——allylic sulfinate; allylic sulfone; allylic acetate; palladium catalyst; sulfinate–sulfone rearrangement; sulfonylation; chiral phosphine ligand; palladium(II) chloride; tetrakis-(triphenylphosphine)palladium; asymmetric induction

Stereochemical studies on palladium-catalyzed reactions in allylic systems[1] have been extensively investigated in the past decade in order to establish the exact mechanisms of allylations and asymmetric induction, especially employing chiral allylic compounds such as chiral allylic acetates,[2] lactones,[3] sulfinates,[4] and sulfones.[4,5] In particular, much attention has been devoted to asymmetric induction in palladium-catalyzed nucleophilic reactions in the presence of chiral ligands such as chiral phosphines, using phenylsulfonylacetate or malonate,[6] β-diketone,[7] and β-ketoester carbanions[8] as nucleophiles.

Quite recently, we have revealed the stereochemistry of thermal[9] and palladium-catalyzed allylic sulfinate–sulfone rearrangements[10] by using readily available allylic sulfinates possessing chirality on the sulfur atoms. We have continued to make efforts to improve the chemical yields and the stereospecificity in synthesis of chiral allylic sulfones. We describe herein details of asymmetric induction in palladium-catalyzed allylic sulfinate-sulfone rearrangements and palladium-catalyzed sulfonylations of allylic acetates effected by chiral phosphine ligands.[11]

Treatment of (*E*)-2-butenyl (±)-*p*-toluenesulfinate (**1a**) with 0.15 eq of tetrakis(triphenylphosphine)palladium in the presence of 0.60 eq of (−)-2,3-*o*-isopropylidene-2,3-dihydroxy-1,4-bis(diphenylphosphino)butane (DIOP)[12] in tetrahydrofuran (THF) at 0 °C for 14 h gave (*R*)-(−)-1-buten-3-yl *p*-tolyl sulfone (**2a**)[9] (73% yield) with 87.0% enantiomeric excess(ee) and an α-rearranged product, 2-butenyl *p*-tolyl sulfone (**3a**) (15% yield). The palladium catalysis of (*Z*)-2-butenyl (±)-*p*-toluenesulfinate (**1b**) under the same conditions afforded an 86.0% ee of the allylic sulfone (*R*)-(−)-**2a** of the same absolute configuration as obtained above. This can be rationalized in terms of transformation of the (*Z*)-allylic intermediate (**4b**) into the more stable one (**4a**) in the equilibrium mediated by the palladium catalyst.

Use of a smaller amount (0.10 and 0.30 eq) of (−)-DIOP in the catalysis of (±)-**1a** afforded (*R*)-(−)-**2a** with much less enantiomeric excess (24%). Catalysis of (±)-**1a**, **b** at lower reaction temperature (−78 °C) led to formation of (*R*)-(−)-**2a** in a slightly lower optical yield.

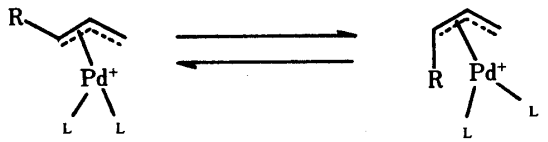


1a: $R^1=CH_3$, $R^2=H$
1b: $R^1=H$, $R^2=CH_3$
1c: $R^1=n\text{-}C_3H_7$, $R^2=H$
1d: $R^1=n\text{-}C_5H_{11}$, $R^2=H$

(*R*)-(−)-**2a**: $R=CH_3$
(*R*)-(−)-**2b**: $R=n\text{-}C_3H_7$
(*R*)-(−)-**2c**: $R=n\text{-}C_5H_{11}$

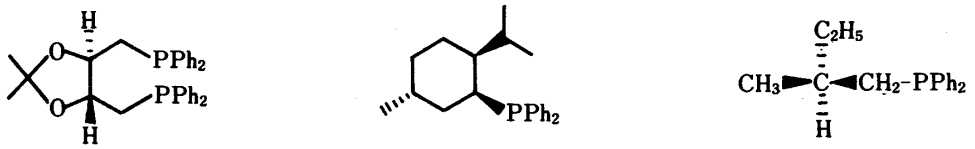
3a: $R=CH_3$
3b: $R=n\text{-}C_3H_7$
3c: $R=n\text{-}C_5H_{11}$

Chart 1



4a **4b**

Chart 2



(−)-DIOP NMDPP (*S*)-MBDPP

Chart 3

TABLE I. The Palladium Catalysis of the Allylic (±)-Sulfinates (**1a—d**) with Chiral Ligands[a]

Sulfinate **1a—d**	Ligand	equivalent	Reaction temp. (°C)	Reaction time (h)	Yield of **2** (%)	$[\alpha]_D$ (EtOH) of **2**	ee (%) of **2**[b]	Yield of **3** (%)
1a	(−)-DIOP	0.1	0	14	65 (**2a**)	−2.4° (*c*, 2.86, 22 °C)	24.0	13 (**3a**)
1a	(−)-DIOP	0.3	0	14	76 (**2a**)	−2.4° (*c*, 2.13, 22 °C)	24.0	15 (**3a**)
1a	(−)-DIOP	0.6	0	14	77 (**2a**)	−8.7° (*c*, 2.85, 22 °C)	87.0	15 (**3a**)
1a	(−)-DIOP	0.6	−78	5	73 (**2a**)	−7.3° (*c*, 2.20, 22 °C)	73.0	15 (**3a**)
1a	NMDPP	1.2	0	14	74 (**2a**)	−7.6° (*c*, 2.66, 21 °C)	76.0	15 (**3a**)
1a	(*S*)-MBDPP	1.2	0	14	72 (**2a**)	−7.3° (*c*, 2.04, 22 °C)	73.0	14 (**3a**)
1b	(−)-DIOP	0.6	0	14	73 (**2a**)	−8.6° (*c*, 2.02, 27 °C)	86.0	15 (**3a**)
1b	(−)-DIOP	0.6	−78	5	51 (**2a**)	−5.3° (*c*, 1.90, 23 °C)	53.0	10 (**3a**)
1c	(−)-DIOP	0.6	0	14	37 (**2b**)	−29.7° (*c*, 1.60, 29 °C)	78.5	55 (**3b**)
1d	(−)-DIOP	0.6	0	14	17 (**2b**)	−30.4° (*c*, 0.85, 25 °C)	83.0	70 (**3b**)

a) The allylic (±)-sulfinates (**1a—d**) were treated with tetrakis(triphenylphosphine)palladium (0.15 eq) in the presence of the chiral ligands in THF. *b*) The enantiomeric excess (%) was calculated from the optical rotations.[9]

Reaction of (±)-**1a** at 0 °C in THF under catalysis with bis(acetonitrile)palladium (II) chloride resulted in complete recovery of the starting material.

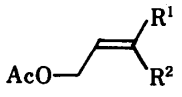
The transformation of (±)-**1a** into (*R*)-(−)-**2a** was studied with other chiral ligands such as neomenthyldiphenylphosphine (NMDPP)[13] and (*S*)-(2-methylbutyl)diphenylphosphine (MBDPP), and the results obtained are summarized in Table I. Among them, catalysis with (−)-DIOP provided (*R*)-(−)-**2a** with the highest enantiomeric excess (87.0%). Similarly, the palladium catalysis of other allylic sulfinates (±)-**1c, d** was carried out in the presence of (−)-DIOP under the same conditions as described above. With the bulkier substituents (R^1 or R^2) in **1a—d**, the ratios of α- to γ-rearranged allylic sulfones were increased in the above palladium catalysis, as shown in Table I.

No equilibrium exists between **2a—c** and **3a—c** in this palladium-catalyzed transformation when THF is used as a solvent without methanol, as mentioned above, which is quite different from the case reported earlier.[14] This was confirmed by complete recovery of the starting chiral allylic sulfones (*R*)-(−)-**2a—c** without any conversion into γ-rearranged products **3a—c**, retaining the optical activity completely, upon treating (*R*)-(−)-**2a—c** with tetrakis (triphenylphosphine)palladium in THF at 0—60 °C.

For much easier access to chiral allylic sulfones, readily obtainable allylic acetates were used instead of the allylic sulfinates in the above reactions.

Studies on palladium-catalyzed sulfonylations of allylic acetates were carried out with various kinds of palladium catalysts; palladium(II) chloride, bis(acetonitrile)palladium(II) chloride, bis(benzonitrile)palladium(II) chloride, and tetrakis(triphenylphosphine)palladium. Treatment of (*E*)-2-butenyl acetate (**5a**) with anhydrous sodium *p*-toluenesulfinate catalyzed by bis(acetonitrile)palladium(II) chloride and bis(benzonitrile)palladium(II) chloride in THF at room temperature led to complete recovery of the starting **5a** without any formation of the expected product. However, heating of **5a** in refluxing THF or benzene in the catalysis by bis(acetonitrile)palladium(II) chloride or bis(benzonitrile)palladium(II) chloride produced allylic sulfones **2a** and **3a**, as listed in Table II, with a 75:25—67:33 ratio of **2a** to **3a**, while the use of palladium(II) chloride in refluxing THF resulted in the lowest yield of the allylic sulfones. Consequently, treatment of **5a** with 0.15 eq of tetrakis(triphenylphosphine)palladium in THF at room temperature led to the highest yield of the allylic sulfones, as shown in Table II.

Reaction of the allylic acetate **6** with anhydrous sodium *p*-toluenesulfinate under catalysis by tetrakis(triphenylphosphine)palladium in THF at room temperature afforded the allylic sulfones **7a,b** in 98% yield as a 77:23 mixture of **7a** and **7b**, which was almost the same ratio (80:20) as that obtained by sulfonylation of geranyl *p*-toluenesulfinate with sodium *p*-toluenesulfinate under the same conditions. It was reported[14b] that the same reaction using,



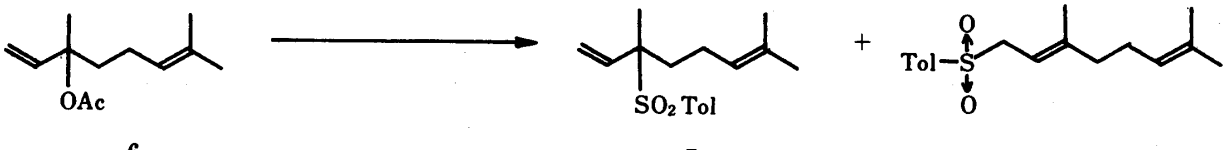
5a: $R^1=CH_3$, $R^2=H$
5b: $R^1=H$, $R^2=CH_3$
5c: $R^1=n\text{-}C_3H_7$, $R^2=H$
5d: $R^1=H$, $R^2=n\text{-}C_3H_7$
5e: $R^1=n\text{-}C_5H_{11}$, $R^2=H$

Chart 4

TABLE II. Studies on Sulfonylation of **5a** with Palladium Catalysts[a]

Palladium catalyst	Solvent	Reaction temp. (°C)	Reaction time (h)	Yield of **2a** (%)	Yield of **3a** (%)
$PdCl_2$[b]	THF	66	18	6	3
$Pd(CH_3CN)_2Cl_2$	THF	66	10	50	17
$Pd(C_6H_5CN)_2Cl_2$	Benzene	80	10	58	28
$Pd(PPh_3)_4$	THF	r.t.	6	73	24

a) (*E*)-2-Butenyl acetate (**5a**) was reacted with anhydrous sodium *p*-toluenesulfinate (2.0 eq) in the presence of palladium catalysts (0.15 eq) and triphenylphosphine (0.66 eq). *b*) Carried out without triphenylphosphine.



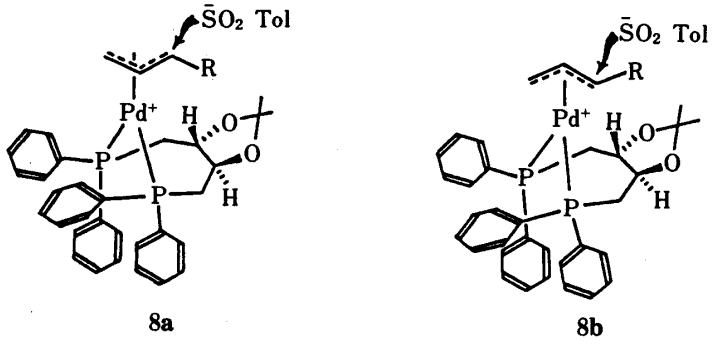
6 **7a** **7b**

Chart 5

TABLE III. The Palladium-Catalyzed Asymmetric Sulfonylation of the Allylic Acetates **5a**—**e**[a]

Acetate **5a**—**e**	Reaction time (h)	Yield of **2** (%)	$[\alpha]_D$ (EtOH) of **2**	ee (%) of **2**[b]	Yield of **3** (%)
5a	6	73 (**2a**)	−8.8° (*c*, 1.93, 29 °C)	88.0	24 (**3a**)
5b	8	70 (**2a**)	−8.8° (*c*, 2.51, 23 °C)	88.0	23 (**3a**)
5c	6	39 (**2b**)	−29.5° (*c*, 1.12, 32 °C)	78.8	59 (**3b**)
5d	7	38 (**2b**)	−26.3° (*c*, 0.95, 22 °C)	70.3	58 (**3b**)
5e	8	21 (**2c**)	−25.3° (*c*, 0.83, 22 °C)	69.6	74 (**3c**)

a) The allylic acetates **5a**—**e** were reacted with sodium *p*-toluenesulfinate (2.0 eq) in the presence of tetrakis(triphenylphosphine)palladium (0.15 eq) and (−)-DIOP (0.6 eq) in THF at room temperature. *b*) The enantiomeric excess (%) was calculated from the optical rotations.[9]



8a **8b**

Chart 6

instead of anhydrous sodium *p*-toluenesulfinate, the hydrate and THF–methanol as a solvent gave the γ-sulfonylated product **7b** without any α-sulfonylated **7a**. However, upon treatment of **7a** with tetrakis(triphenylphosphine)palladium in THF at room temperature overnight, no transformation of **7a** into **7b** was observed, in contrast to the case reported previously,[14b] resulting in complete recovery of **7a**. It is very important to use metanol as a solvent for dissolving the hydrate of sodium *p*-toluenesulfinate completely; the anhydrous sodium *p*-toluenesulfinate was more soluble in THF. Moreover, it should be noted that one of the most important factors determining the reaction course would be participation of methanol in the palladium catalysis.

Next, palladium-catalyzed asymmetric sulfonylations of allylic acetates were executed using several kinds of allylic acetates and chiral phosphine ligands. The reaction of **5a** with sodium *p*-toluenesulfinate in the presence of tetrakis(triphenylphosphine)palladium (0.15 eq) and (−)-DIOP (0.60 eq) in THF at room temperature for 6 h gave (*R*)-(−)-**2a** in 73% yield with 88.0% ee. The sulfonylation of (*Z*)-2-butenyl acetate (**5b**) with sodium *p*-toluenesulfinate under the same conditions provided the allylic sulfone (*R*)-(−)-**2a** of the same absolute configuration as obtained in the (*E*)-system (**5a**), with 88.0% ee.

The palladium-catalyzed reactions of both (*E*)- and (*Z*)-2-hexenyl acetate (**5c**) and (**5d**) with sodium *p*-toluenesulfinate produced (*R*)-(−)-1-hexen-3-yl *p*-tolyl sulfone (**2b**)[9] in 39 and 38% yields with 78.8 and 70.3% ee, as well as 2-hexenyl *p*-tolyl sulfone (**3b**) (59 and 58% yields, respectively). This can be reasonably explained in terms of the equilibrium between **4a** and **4b**, in the same way as mentioned earlier in the catalysis of the sulfinates **1a**, **b**. The results obtained by asymmetric sulfonylations of **5a**—**e** with (−)-DIOP are summarized in Table III.

The mechanistic pathway for this asymmetric induction with (−)-DIOP is considered to be as follows. In the presence of (−)-DIOP, a seven-membered intermediate would be formed by replacement of the ligand with (−)-DIOP and coordination of the palladium catalyst with

the allylic systems. The preferred conformations in the intermediary palladium complex would be the diagonally coordinated states **8a** and **8b**. In these states, more severe steric interference is observed in **8a** between the substituent R and one of the oxygen moieties of (−)-DIOP. Therefore, the *p*-toluenesulfonyl group reacts from the top side of the preferred intermediate **8b**, resulting in the formation of (*R*)-(−)-**2a**—**c** with high enantiomeric excess.

Thus, this novel method provides a new entry to synthetically valuable optically active allylic sulfones.

Experimental

Thin-layer or preparative thick layer plates were made of Merck Silica gel 60PF-254 activated by drying at 140 °C for 3.5 h.

Allylic sulfinates (±)-**1a**—**d** were prepared according to the method reported previously.[10b] Allylic acetates **5a**—**e** were obtained in the normal way and linalyl acetate is commercially available.

Palladium-Catalyzed Reactions of Allylic (±)-*p*-Toluenesulfinates in the Presence of Chiral Phosphine Ligands: General Procedure——A dry 25 ml two-necked flask equipped with a septum inlet and a magnetic stirring bar, and containing 41 mg (0.04 mmol) of tetrakis(triphenylphosphine)palladium, was flushed with nitrogen, and maintained under a positive pressure of nitrogen. A solution of chiral phosphine ligands ((−)-DIOP, NMDPP, and (*S*)-MBDPP, 0.14 mmol) in 3 ml of THF was added to the flask, and the mixture was stirred at 0 °C for 30 min. A solution of allylic (±)-sulfinates **1a**—**d** in 3 ml of THF was added. The reaction mixture was stirred at 0°C for 14 h, and then diluted with ether. The ethereal solution was washed with saturated aqueous NaCl, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residual oil was subjected to preparative thin layer chromatography (TLC) (ether-hexane, 1 : 2) to give (*R*)-(−)-**2a**—**c** and **3a**—**c**. The yields and the optical rotations of the products are summarized in Table I.

The infrared (IR), nuclear magnetic resonance (NMR), and mass (MS) spectral data were identical with those of the products prepared by other methods reported previously.[10b]

Palladium-Catalyzed Asymmetric Sulfonylations of Allylic Acetates 5a—d with Anhydrous Sodium *p*-Toluenesulfinate in the Presence of Chiral Phosphine Ligands: General Procedure——A dry 25 ml two-necked flask equipped with a septum inlet and a magnetic stirring bar, and containing 58 mg (0.05 mmol) of tetrakis(triphenylphosphine)palladium, was flushed with nitrogen, and maintained under a positive pressure of nitrogen. A solution of 100 mg (0.20 mmol) of (−)-DIOP in 1.5 ml of THF was added to the flask. After stirring of the mixture at 0 °C for 30 min, a solution of an allylic acetate **5a**—**e** (0.33 mmol) in 1.5 ml of THF was added at room temperature, followed by dropwise addition of a suspension of 119 mg (0.67 mmol) of anhydrous sodium *p*-toluenesulfinate in 2 ml of THF. The reaction mixture was stirred at room temperature for 6—8 h, and then diluted with ether. The ethereal solution was washed with saturated aqueous NaCl, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The crude products were subjected to preparative TLC (ether–hexane, 1 : 2) to give (*R*)-(−)-**2a**—**c** and **3a**—**c**. The yields, the optical rotations, and the optical yields of the products are listed in Table III.

The IR, NMR, and MS spectral data were identical with those of samples prepared by another method.[10b]

Palladium-Catalyzed Sulfonylation of Linalyl Acetate (6) with Anhydrous Sodium *p*-Toluenesulfinate——A suspension of 182 mg (1.02 mmol) of anhydrous sodium *p*-toluenesulfinate in 3 ml of THF was added to a mixture of tetrakis(triphenylphosphine)palladium (88 mg, 0.08 mmol), triphenylphosphine (88 mg, 0.34 mmol), and **6** (100 mg, 0.51 mmol) in 4 ml of THF at room temperature. The reaction mixture was stirred at room temperature for 16 h, and then diluted with ether. The ethereal solution was washed with saturated aqueous NaCl, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residual oil was subjected to preparative TLC (ether–hexane 1 : 2) to give sulfonylated products **7** (146 mg, 98% yield) as a 77 : 23 mixture of linalyl *p*-tolyl sulfone (**7a**) and geranyl *p*-tolyl sulfone (**7b**). The IR and NMR spectra were identical with those of the samples prepared by other methods.[10b]

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