Asymmetric Induction Reactions. IV.[1] Palladium-Catalyzed Asymmetric Allylations of Chiral Enamines Bearing Phosphine Groups[2]

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The palladium-catalyzed asymmetric allylations of chiral enamines, derived from (*S*)-2-(diphenylphosphinomethyl)pyrrolidine, produced optically active α-allyl carbonyl compounds in high optical yields. The phosphino group in the chiral enamines presumably serves as a chiral ligand in these palladium-catalyzed reactions. In the transition states of π-allylpalladium complexes coordinated with the intramolecular phosphine group, the anionic counterparts or allylating reagents are considered to play an important role in controlling of the grade of the enantioselectivity.

Keywords asymmetric allylation; palladium catalyst; enantioselectivity; phosphine ligand; allylating reagent; chiral enamine

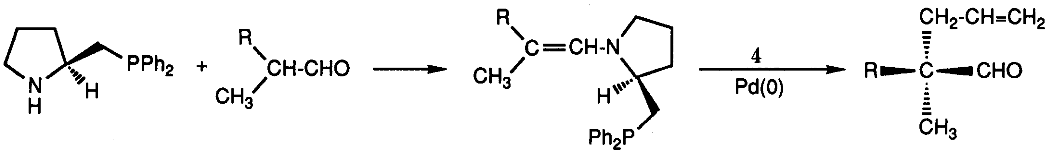
Recently much attention has been paid to the development of new methodologies for asymmetric induction with high enantioselectivity,[3] especially using transition metal catalysts.[4] Particular interest has been focused on the mechanisms of palladium-catalyzed reactions, especially in allylic systems with chiral models involving chiral sulfinates,[5] esters of chiral allylic alcohols,[6] and chiral phosphine ligands.[7] We have already explored new methods for asymmetric α-allylation of carbonyl compounds *via* π-allylpalladium complexes of chiral enamines,[8] imines,[9] or amides[10] derived from (*S*)-proline and other (*S*)-α-amino acid allyl esters, and suggested possible mechanisms of the asymmetric induction. Asymmetric alkylation with chiral enamines provides a useful method for preparation of optically active α-alkyl carbonyl compounds, as reported previously by one (K. H.) of us.[11] Accordingly, palladium-catalyzed reactions of chiral enamines involving phosphine groups have attracted much interest, since the phosphine groups would presumably serve as chiral ligands in the palladium catalysis and therefore different stereochemical results would be expected, compared with those obtained by the previous chiral enamine alkylation methods.[11]

As a chiral secondary amine with a phosphine group, we used (*S*)-2-(diphenylphosphinomethyl)pyrrolidine (**1**)[12] which was easily obtainable from (*S*)-proline. The chiral enamine (*S*)-**3a** was prepared by azeotropic dehydration of (*S*)-**1** and 2-phenylpropanal (**2a**) in refluxing benzene for 4 h using a Dean–Stark apparatus. Reaction of the chiral enamine (*S*)-**3a** with allyl acetate (**4a**) (2.0 eq) was carried out in tetrahydrofuran (THF) at room temperature or 66 °C for 45 or 19 h in the presence of tetrakis(triphenylphosphine)palladium [$Pd(PPh_3)_4$] (0.2 eq), followed by hydrolysis of the allylated enamine with 10% aqueous HCl–benzene (at 80 °C, for 1 h), giving (*R*)-(−)-2-methyl-2-phenyl-4-pentenal (**5a**) with 52 or 18% enantiomeric excess in 80 or 86% yield, respectively. The absolute configuration of the product (−)-**5a** has already been determined as (*R*)-(−)-**5a** by us.[8b] The enantiomeric excess (e.e.) of the product was determined by nuclear magnetic resonance (NMR) spectral analysis with a shift reagent, tris[3-(heptafluoropropylhydroxymethylene)-(+)-camphorato]europium (III) [$Eu(hfc)_3$].

In order to improve the chemical and optical yields of the product, stereochemical studies on this allylation have been attempted employing various other allylating reagents such as allyl carboxylates (**4a**—**e**), sulfonates (**4f**, **g**), and halides (**4h**—**j**). The results are summarized in Table I.

The direct reactions of (*S*)-**3a** with **4a**—**j** without the palladium catalyst, even in refluxing THF, gave none of the expected products. On the other hand, the direct reactions of (*S*)-**3a** with **4h**—**j** without the catalyst in refluxing THF produced (*S*)-(+)-**5a** in extremely lower optical yields (6—13%). However, the reactions at room temperature afforded no α-allylated aldehyde.

Therefore, the results listed in Table I indicate that the



(*S*)-**1**

2a : R = C_6H_5
2b : R = *p*-$Bu^tC_6H_4CH_2$
2c : R = C_2H_5

(*S*)-**3a**—**c**

(*R*)-**5a** : R = C_6H_5
(*R*)-**5b** : R = *p*-$Bu^tC_6H_4CH_2$
(*S*)-**5c** : R = C_2H_5

$CH_2=CH-CH_2-X$

4a : X = AcO
4b : X = $C_6H_5CO_2$
4c : X = *p*-$NO_2C_6H_4CO_2$
4d : X = α-$C_{10}H_7CO_2$
4e : X = β-$C_{10}H_7CO_2$
4f : X = *p*-$CH_3C_6H_4SO_3$
4g : X = *o*-$CH_3C_6H_4SO_3$
4h : X = Cl
4i : X = Br
4j : X = I

Chart 1

anionic counterparts, presumably coordinated with the palladium catalyst, do affect the asymmetric induction in the palladium-catalyzed reactions. A remarkably large effect of the anionic counterparts of the allylating reagents on the asymmetric induction was observed. The optical yields increased with increasing steric bulkiness of the anionic counterparts (X) in allyl carboxylates and sulfonates. Exceptionally, allyl carboxylates having very large substituents such as α- or β-naphthoyl groups provided lower enantioselectivity. In the palladium-catalyzed reactions with allyl halides (**4i**—**j**), contrary to expectation, rather lower enantioselectivity was observed with the use of allyl iodide. Among the allylating reagents examined, the palladium-catalyzed reaction of (*S*)-**3a** with allyl bromide provided the highest optical yields of (*R*)-**5a**. This means that the steric character of the bromine atom is crucial for the asymmetric allylation in this system, and the reactivity of allylating reagents plays an important role in controlling the grade of the asymmetric induction. The effect of the anionic counterparts on the asymmetric induction can not be completely rationalized at this stage. It is presumably related to the coordinating ability of the anionic counterparts to the palladium catalyst, and also to the steric bulk.

TABLE I. The Palladium-Catalyzed Asymmetric Allylation of (*S*)-**3a**—**c**[a]

Enamine (*S*)-3	4	Reaction temp. (°C)	Reaction time (h)	Product	Yield (%)[b]	$[\alpha]_D$ (MeOH)	ee (%)[c]
3a	**4a**	66	19	(*R*)-**5a**	86	−6.2°	18
3a	**4a**	40	19	(*R*)-**5a**	74	−12.3°	35
3a	**4a**	r.t.	45	(*R*)-**5a**	80	−18.3°	52
3a	**4a**	66	19	(*S*)-**5a**	79[d]	+3.2°	8
3a	**4a**	40	19	(*S*)-**5a**	75[d]	+3.8°	10
3a	**4a**	r.t.	45	(*S*)-**5a**	61[d]	+5.8°	15
3a	**4b**	66	19	(*R*)-**5a**	83	−11.7°	31
3a	**4b**	40	19	(*R*)-**5a**	88	−14.0°	37
3a	**4b**	r.t.	45	(*R*)-**5a**	78	−21.0°	53
3a	**4c**	66	19	(*R*)-**5a**	82	−13.6°	36
3a	**4c**	40	19	(*R*)-**5a**	73	−16.7°	44
3a	**4c**	r.t.	45	(*R*)-**5a**	83	−27.0°	71
3a	**4d**	66	19	(*R*)-**5a**	71	−8.0°	21
3a	**4d**	40	19	(*R*)-**5a**	78	−12.0°	32
3a	**4d**	r.t.	45	(*R*)-**5a**	65	−17.2°	45
3a	**4e**	66	19	(*R*)-**5a**	70	−5.0°	13
3a	**4e**	40	19	(*R*)-**5a**	77	−11.9°	32
3a	**4e**	r.t.	45	(*R*)-**5a**	68	−20.3°	53
3a	**4f**	66	19	(*R*)-**5a**	77	−17.8°	47
3a	**4f**	40	19	(*R*)-**5a**	85	−22.9°	58
3a	**4f**	r.t.	45	(*R*)-**5a**	77	−30.0°	79
3a	**4g**	66	19	(*R*)-**5a**	83	−18.0°	47
3a	**4g**	40	19	(*R*)-**5a**	85	−21.3°	55
3a	**4g**	r.t.	45	(*R*)-**5a**	80	−32.0°	84
3a	**4h**	66	19	(*R*)-**5a**	92	−5.2°	14
3a	**4h**	r.t.	45	(*R*)-**5a**	90	−23.8°	63
3a	**4h**	66	19	(*S*)-**5a**	81[e]	+2.4°	6
3a	**4i**	66	19	(*R*)-**5a**	90	−8.0°	21
3a	**4i**	r.t.	45	(*R*)-**5a**	77	−33.3°	88
3a	**4i**	66	19	(*S*)-**5a**	60[e]	+3.3°	9
3a	**4j**	66	19	(*R*)-**5a**	91	−4.1°	11
3a	**4j**	r.t.	45	(*R*)-**5a**	94	−20.5°	54
3a	**4j**	66	19	(*S*)-**5a**	77[e]	+5.1°	13
3b	**4a**	66	19	(*R*)-**5b**	91	+1.9°	35
3b	**4a**	40	19	(*R*)-**5b**	84	+2.5°	46
3b	**4a**	r.t.	45	(*R*)-**5b**	82	+3.5°	64
3b	**4f**	66	19	(*R*)-**5b**	98	+2.3°	42
3b	**4f**	40	19	(*R*)-**5b**	87	+3.1°	56
3b	**4f**	r.t.	45	(*R*)-**5b**	88	+4.4°	80
3b	**4g**	66	19	(*R*)-**5b**	98	+2.0°	36
3b	**4g**	40	19	(*R*)-**5b**	81	+3.8°	69
3b	**4g**	r.t.	45	(*R*)-**5b**	85	+4.1°	75
3b	**4i**	66	19	(*R*)-**5b**	87	+2.7°	49
3b	**4i**	40	19	(*R*)-**5b**	90	+3.8°	69
3b	**4i**	r.t.	45	(*R*)-**5b**	85	+4.8°	87
3c	**4a**	66	19	(*S*)-**5c**	81	−4.0°	18
3c	**4a**	40	19	(*S*)-**5c**	79	−7.2°	33
3c	**4a**	r.t.	45	(*S*)-**5c**	85	−10.2°	46
3c	**4f**	66	19	(*S*)-**5c**	93	−6.7°	30
3c	**4f**	40	19	(*S*)-**5c**	89	−9.4°	43
3c	**4f**	r.t.	45	(*S*)-**5c**	88	−13.8°	52
3c	**4g**	66	19	(*S*)-**5c**	92	−10.1°	36
3c	**4g**	40	19	(*S*)-**5c**	85	−12.4°	47
3c	**4g**	r.t.	45	(*S*)-**5c**	81	−14.8°	60
3c	**4i**	66	19	(*S*)-**5c**	82	−7.4°	34
3c	**4i**	40	19	(*S*)-**5c**	79	−9.8°	44
3c	**4i**	r.t.	45	(*S*)-**5c**	83	−11.4°	52

a) The reactions of **3a**—**c** with **4a**—**j** were carried out in THF in the presence of $Pd(PPh_3)_4$(0.2 eq) followed by hydrolysis with 10% aqueous HCl–benzene for 1 h. *b*) The corrected yields based on the recovered starting materials are listed. *c*) The enantiomeric excess (ee %) was calculated by NMR analysis using a shift reagent [$Eu(hfc)_3$] and from the optical rotation of optically pure (*R*)-**5a**, $[\alpha]_D$ −38.0° (MeOH); (*R*)-**5b**, $[\alpha]_D$ +5.5° (MeOH) and (*S*)-**5c**, $[\alpha]_D$ −22.1° (MeOH). *d*) The reactions were carried out in the presence of $Pd(dba)_2$(0.2 eq). *e*) The reactions were carried out without palladium catalyst. r.t. = room temperature.

It should be noted that the palladium catalysts have an important effect on the asymmetric induction: the use of bis(dibenzylideneacetone)palladium [$Pd(dba)_2$] resulted in a much lower optical yield of (*S*)-**5a** in the reaction of (*S*)-**3a** with allyl acetate than that obtained with $Pd(PPh_3)_4$.

Asymmetric allylations of other chiral aldehyde-enamines (*S*)-**3b**, **c**, derived from (*S*)-**1** and **2b**, **c**, were attempted using allylating reagents **4a**, **f**, **g**, **i**. The reactions of (*S*)-**3b**, **c** with **4a**, **f**, **g**, **i** were carried out in THF in the presence of Pd$(PPh_3)_4$ (0.2 eq), followed by heating in 10% aqueous HCl and benzene for 1 h, to produce (*R*)-(+)-**5b** and (*S*)-(−)-**5c**. The results are summarized in Table I. The absolute configurations of the aldehydes were deduced on the basis of the mechanistic pathway proposed later. The enantiomeric excess of the products was determined by NMR spectral analysis with a shift reagent [$Eu(hfc)_3$]. Higher enantiomeric excess of the products was observed on treatment with **4f**, **g**, **i**, as shown in Table I.

TABLE II. The Palladium-Catalyzed Asymmetric Allylations of (*S*)-**6** and **9**[a]

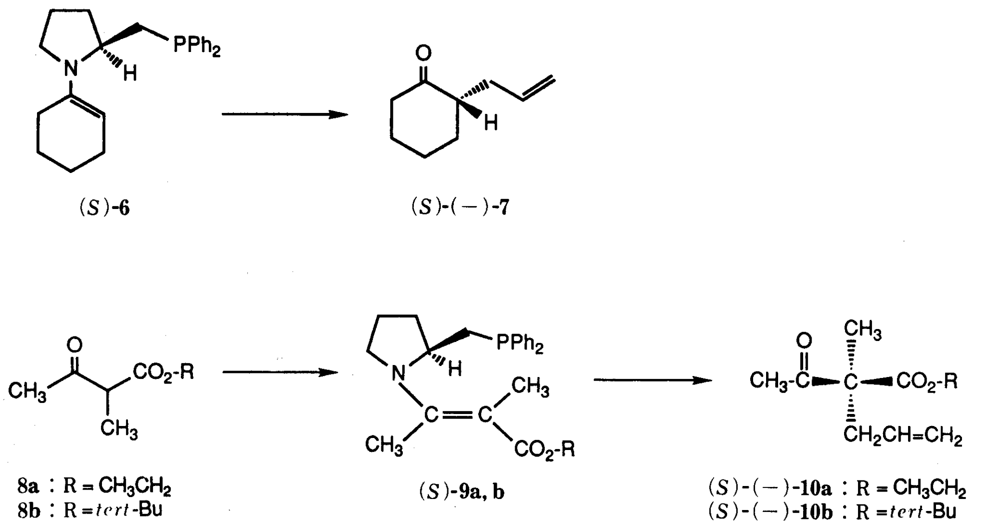
Enamine	4	Product	Yield (%)[b]	Product $[\alpha]_D$ (MeOH or $CHCl_3$)	ee (%)[c]
(*S*)-**6**	**4a**	(*S*)-**7**	77	−4.2°	27
(*S*)-**6**	**4b**	(*S*)-**7**	83	−4.4°	28
(*S*)-**6**	**4c**	(*S*)-**7**	70	−7.3°	46
(*S*)-**6**	**4f**	(*S*)-**7**	67	−10.3°	65
(*S*)-**6**	**4g**	(*S*)-**7**	62	−11.2°	71
(*S*)-**6**	**4i**	(*S*)-**7**	68	−9.6°	61
(*S*)-**9a**	**4a**	(*S*)-**10a**	77	−11.0°	37
(*S*)-**9b**	**4a**	(*S*)-**10b**	85	−17.4°	77
(*S*)-**9b**	**4b**	(*S*)-**10b**	84	−14.1°	62
(*S*)-**9b**	**4c**	(*S*)-**10b**	84	−15.2°	67
(*S*)-**9b**	**4f**	(*S*)-**10b**	89	−19.0°	84
(*S*)-**9b**	**4g**	(*S*)-**10b**	83	−19.3°	85
(*S*)-**9b**	**4i**	(*S*)-**10b**	78	−17.8°	78

a) The reactions of (*S*)-**6** or -**9a**, **b** with **4** were carried out in refluxing THF for 19 h in the presence of $Pd(PPh_3)_4$ (0.2 eq) followed by hydrolysis with aqueous $AcONa–AcOH–H_2O$–benzene. *b*) The corrected yields based on the recovered starting materials are listed. *c*) The enantiomeric excess (ee %) was determined on the basis of the optical rotation of optically pure (*S*)-**7** ($[\alpha]_D$ −15.8° (MeOH)),[15] (*S*)-**10a** ($[\alpha]_D$ −29.7° ($CHCl_3$)),[14] and (*S*)-**10b** ($[\alpha]_D$ −22.7° ($CHCl_3$)).

This method was applicable to chiral keto-enamines. The chiral keto-enamine (*S*)-**6**, prepared from (*S*)-**1** and cyclohexanone, was reacted with **4** in the presence of Pd $(PPh_3)_4$ (0.2 eq) in refluxing THF for 19 h, followed by hydrolysis with AcONa–AcOH–H_2O–benzene (at room temperature for 1 h), giving (*S*)-2-allylcyclohexanone (**7**).[8a,11] Rather high optical yields were observed in the reactions with allyl tosylates (**4f, g**) and bromide (**4i**), as shown in Table II. The chiral enamine (*S*)-**9a, b**, derived from (*S*)-**1** and ethyl or *tert*-butyl 2-methylacetoacetate (**8a**[13] or **8b**), was reacted with **4** under the same conditions as described above to give ethyl or *tert*-butyl (*S*)-2-allyl-2-methylacetoacetate (**10a**[14] or **10b**) in the optical yields listed in Table II. The absolute configuration of **10b** and the optical rotation of optically pure **10b** were determined by chemical correlation to (*S*)-(−)-**10a** of known absolute configuration[14] *via* 2-acetyl-2-methyl-4-pentenyl benzoate. High optical yields of (*S*)-**10b** were obtained when (*S*)-**9b** was reacted with **4f** and **4g** in refluxing THF.

The stereochemistry of these reactions was rationalized as follows. The palladium-catalyzed reaction of (*S*)-**3a** with **4a**—**j** provided (*R*)-**5a** of the same absolute configuration as that of the product *via* (*S*)-proline allyl ester enamine.[8b] Therefore, the allylation of (*S*)-**3a** is considered to proceed *via* a π-allylpalladium complex intramolecularly coordinated with the phosphine ligand.

The geometrical isomers **12** of the enamines (*S*)-**3** and (*S*)-**9** are preferred to the other isomers **11** because of the steric hindrance between the amino part and the large substituent (R^2) in **11**. The conformers **13** seem preferable to **12** from the viewpoint of steric interaction between the diphenylphosphinomethyl and the methyl groups in **12**. Therefore the preferred conformers **13** formed the π-allylpalladium complexes **14** coordinated with the phosphine group and the counterparts (X), and allylation then occurred *via* the palladium complexes from the bottom side as depicted in **14**, providing (*R*)-**5a, b**, (*S*)-**5c** or (*S*)-**10**. The steric effect of the anionic counterparts (X), presumably bonded to the palladium catalyst, is manifested at this stage. The allylating reagents (*e.g.* **4d** and **4e**) having overlarge anionic counterparts (X) could not be completely coordinated with the phosphine groups and therefore partial allylations *via* the π-allylpalladium complexes **14** would occur, along with the direct allylations from the back side of the chiral part in **13**, providing somewhat lower



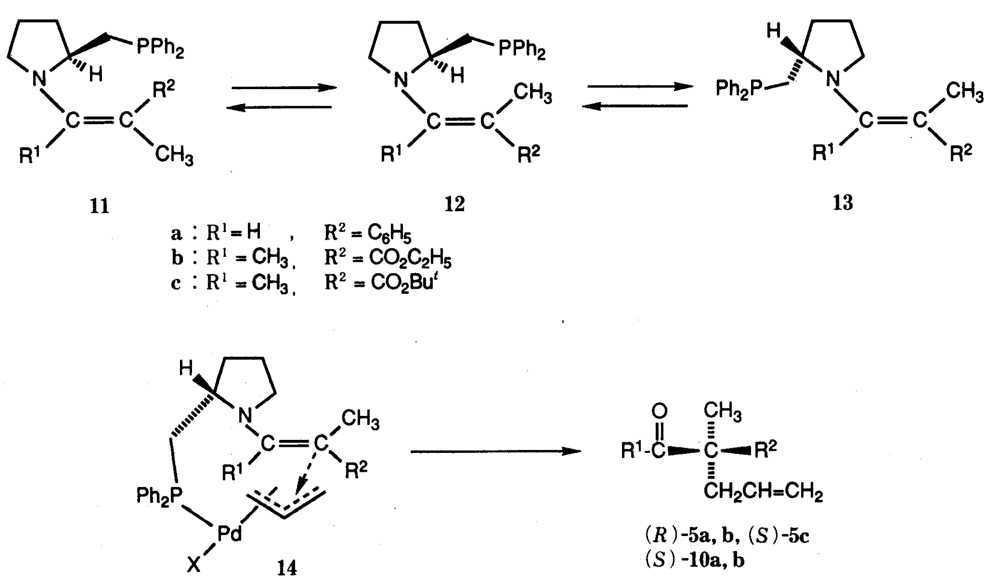
(*S*)-**6**
(*S*)-(−)-**7**

8a : R = CH_3CH_2
8b : R = *tert*-Bu

(*S*)-**9a, b**

(*S*)-(−)-**10a** : R = CH_3CH_2
(*S*)-(−)-**10b** : R = *tert*-Bu

Chart 2



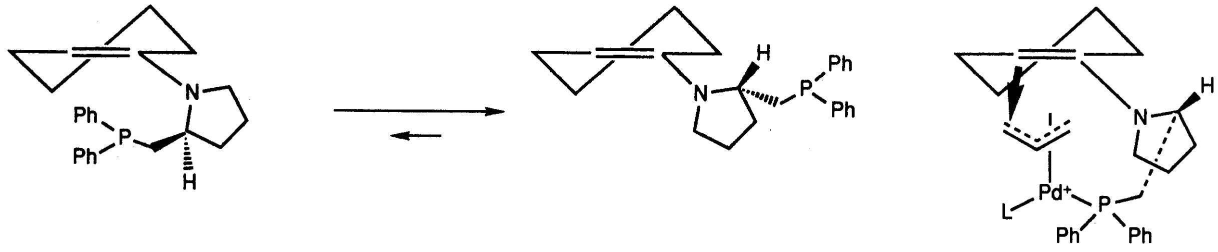
11 **12** **13**

a : $R^1 = H$, $R^2 = C_6H_5$
b : $R^1 = CH_3$, $R^2 = CO_2C_2H_5$
c : $R^1 = CH_3$, $R^2 = CO_2Bu^t$

14

(*R*)-**5a, b**, (*S*)-**5c**
(*S*)-**10a, b**

Chart 3



15a **15b** **16**

Chart 4

enantioselectivity in these palladium-catalyzed reactions. The allylations catalyzed by Pd(dba)$_2$ resulted in the formation of (*S*)-**5a** of reversed absolute configuration with lower enantioselectivity, since the formation of the π-allylpalladium complexes **14** coordinated by the phosphine ligand would not be easily attainable with Pd(dba)$_2$ and the direct allylation from the back side of the chiral part in **13** would be slightly preferable to that *via* **14**.

The great difference of the stereochemical results in the allylations with allyl halides can be rationalized in terms of the reactivity and the steric bulkiness of the halides. The high reactivity of allyl iodide allows partial direct allylation of the enamine without formation of the π-allylpalladium complexs **14** by coordination with the phosphine group, resulting in the lower enantioselectivity.

A similar explanation is applicable to the cyclohexanone enamine system (*S*)-**6**. The palladium-catalyzed reaction of (*S*)-**6** would proceed preferentially *via* the π-allylpalladium complex **16** coordinated with the phosphine group in the conformationally most stable from **15b**, producing (*S*)-**7** with the high enantioselectivity, since **15b** would be preferred to **15a** because of steric hindrance between the diphenylphosphinomethyl group and the olefinic hydrogen atom in **15a**.[11]

Thus, this method provides different stereochemical results, compared with those obtained by the previous method *via* chiral enamines.[11] Therefore we can control the stereochemistry of the products by selecting the amino moiety in chiral enamines. Accordingly, this method is useful for asymmetric α-allylation of carbonyl compounds and is also advantageous for organic synthesis, because the chiral auxiliary amine used as the starting chiral source can be efficiently recovered and recycled. Furthermore, it is noteworthy that the anionic counterparts of allylating reagents have a great effect on the asymmetric induction in these palladium-catalyzed reactions. This is the first demonstration of the importance of participation of anionic counterparts of allylating reagents in palladium-catalyzed asymmetric allylations.

Experimental

Thin-layer or preparative thick layer plates (preparative TLC) were made of Merck Silica gel 60PF-254 activated by drying at 140 °C for 3.5 h. Infrared (IR) spectra were obtained in the indicated state with a Hitachi 215 spectrometer and a JASCO DR-81 Fourier-transform infrared spectrometer. NMR spectra were determined in indicated solvent with a Hitachi R-24B high-resolution NMR spectrometer and a JEOL JNM-PMX 60si high-resolution NMR spectrometer (60 MHz); chemical shifts are given in ppm from tetramethylsilane as an internal standard. Splitting patterns are designated as s, singlet; d, doublet; q, quartet; m, multiplet. Mass spectra (MS) were taken on JEOL JMS-DX 303/JMA-DA 5000 system.

Synthesis of (*S*)-2-(Diphenylphosphinomethyl)pyrrolidine (1) (*S*)-*N*-*tert*-Butoxycarbonylproline Ethyl Ester: Potassium carbonate (6.4 g, 0.050 mol) was added to a solution of *N*-*tert*-butoxycarbonylproline (5.0 g, 0.025 mol) in 400 ml of acetone at room temperature. Ethyl iodide (18.6 ml, 0.250 mol) was added to the above suspension. The whole was stirred at room temperature for 16 h. The reaction mixture was filtered and the precipitates were washed with ether. The filtrates were combined and concentrated *in vacuo*. The residual oil was dissolved with ether. The solution was washed with saturated aqueous NaHCO$_3$ and saturated aqueous NaCl, dried over anhydrous Na$_2$SO$_4$, and concentrated *in vacuo*. The curde product was subjected to distillation under reduced pressure to give (*S*)-*N*-*tert*-butoxycarbonylproline ethyl ester (5.6 g, quantitative yield): bp 170 °C (4 mmHg), $[\alpha]_D^{23}$ −38.7° (c=2.3, EtOH). IR ν_{max}^{film} cm^{-1}: 1760 (ester), 1700 (C=O). NMR (CCl$_4$) δ: 1.03—1.63 (12H, m, CH$_2$C$\underline{H}_3$, C(C$\underline{H}_3$)$_3$), 1.70—2.53 (4H, m, CH$_2$CH$_2$), 3.16—3.86 (3H, m, CH$_2$N, NCH), 4.26 (2H, q, J=8, 8 Hz, C$\underline{H}_2$CH$_3$). MS m/z: 243 (M$^+$). Exact mass determination: 243.1479 (Calcd for $C_{12}H_{21}NO_4$: 243.1470).

(*S*)-*N*-*tert*-Butoxycarbonylprolinol: Lithium aluminum hydride (1.0 g, 0.033 mol) was added to a solution of (*S*)-*N*-*tert*-butoxycarbonylproline ethyl ester (4.8 g, 0.023 mol) in 100 ml of THF cooled to 0 °C. The reaction mixture was stirred at 0 °C for 16 h and then quenched with H$_2$O (3.0 ml) and 10% aqueous NaOH (0.9 ml). The mixture was diluted with ether and then refluxed for 1 h. The precipitates were filtered off and washed with ether. The filtrates were combined and concentrated *in vacuo*. The crude product was subjected to distillation under reduced pressure to give (*S*)-*N*-*tert*-butoxycarbonylprolinol (3.8 g, 96% yield): bp 150 °C (4 mmHg), $[\alpha]_D^{24}$ −30.8° (c=1.3, EtOH). IR ν_{max}^{film} cm^{-1}: 3370 (OH), 1700 (C=O). NMR (CCl$_4$) δ: 1.50 (9H, s, C(CH$_3$)$_3$), 1.66—2.33 (4H, m, CH$_2$CH$_2$), 3.00—4.66 (6H, m, CH$_2$NCH, CH$_2$OH). MS m/z: 201 (M$^+$). Exact mass determination; 201.1389 (Calcd for $C_{10}H_{19}NO_3$: 201.1364).

(*S*)-*N*-*tert*-Butoxycarbonylprolinol *p*-Toluenesulfonate: *p*-Toluenesulfonyl chloride (4.3 g, 0.023 mol) was added to a solution of (*S*)-*N*-*tert*-butoxycarbonylprolinol (3.8 g, 0.019 mol) in 10 ml of anhydrous pyridine at 0 °C. The reaction mixture was stirred at 0 °C for 4 h, and then diluted with ether. The solution was washed with 10% aqueous HCl, saturated aqueous NaHCO$_3$, and saturated aqueous NaCl, dried over anhydrous Na$_2$SO$_4$, and concentrated *in vacuo*. The crude product was subjected to preparative TLC (ether–hexane, 1 : 2) to give (*S*)-*N*-*tert*-butoxycarbonylprolinol *p*-toluenesulfonate (6.1 g, 91% yield): $[\alpha]_D^{28}$ −40.8° (c=1.8, EtOH). IR ν_{max}^{film} cm^{-1}: 1680 (C=O), 1600 (aromatic), 1180 (OSO$_2$). NMR (CCl$_4$) δ: 1.36 (9H, s, C(CH$_3$)$_3$), 1.60—2.23 (4H, m, CH$_2$CH$_2$), 2.43 (3H, s, C$_6$H$_4$C$\underline{H}_3$), 3.06—3.30 (2H, m, CH$_2$N), 3.60—4.26 (3H, m, NCH, CH$_2$O), 7.10—7.86 (4H, m, C$_6$H$_4$). MS m/z: 355 (M$^+$). Exact mass determination; 355.1439 (Calcd for $C_{17}H_{25}NO_5S$: 355.1452).

(*S*)-*N*-*tert*-Butoxycarbonyl-2-(diphenylphosphinomethyl)pyrrolidine: A mixture of sodium (0.8 g, 0.034 gatom) and chlorodiphenylphosphine (4.2 ml, 0.023 mol) in 20 ml of dioxane was refluxed for 15 h under a nitrogen atmosphere. After cooling, the solution was added to a solution of (*S*)-*N*-*tert*-butoxycarbonylprolinol *p*-toluenesulfonate (1.0 g, 0.003 mol) in THF (10 ml) at room temperature. The reaction mixture was stirred at room temperature for 19 h and then diluted with ether. The solution was washed with saturated aqueous NaCl, dried over anhydrous Na$_2$SO$_4$, and concentrated *in vacuo*. The crude product was subjected to preparative TLC (ether–hexane, 2 : 1) to give (*S*)-*N*-*tert*-butoxycarbonyl-2-(diphenylphosphinomethyl)pyrrolidine (0.9 g, 93% yield): $[\alpha]_D^{24}$ −45.8° (c=1.7, EtOH). IR ν_{max}^{film} cm^{-1}: 1680 (C=O), 1600 (aromatic). NMR (CCl$_4$) δ: 1.43 (9H, s, C(CH$_3$)$_3$), 1.60—2.30 (4H, m, CH$_2$CH$_2$), 2.50—4.60 (5H, m, CH$_2$NCH, CH$_2$P), 7.10—8.10 (10H, m, P(C$_6$H$_5$)$_2$). MS m/z: 369(M$^+$). Exact mass determination: 369.2119 (Calcd for $C_{22}H_{28}NO_2P$: 369.2108).

(*S*)-**1**: (*S*)-*N*-*tert*-Butoxycarbonyl-2-(diphenylphosphinomethyl)pyrrolidine (0.7 g, 0.019 mol) was dissolved in 10 ml of freshly distilled trifluoroacetic acid at 0 °C and the solution was stirred for 2 h. Then trifluoroacetic acid was removed *in vacuo* to leave (*S*)-2-(diphenylphosphinomethyl)pyrrolidinium trifluoroacetate. The salt was dissolved in 20 ml of chloroform, followed by addition of 10% aqueous ammonia. The mixture was stirred for 10 min and then diluted with chloroform. The solution was washed with saturated aqueous NaCl, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The crude product was subjected to distillation under reduced pressure to give (*S*)-2-(diphenylphosphinomethyl)pyrrolidine[12] (0.5 g, 93% yield) as a yellow oil: bp 220°C (4 mmHg), $[\alpha]_D^{25}$ −27.9° (*c*=2.9, EtOH) [lit.[12] bp 148 °C (0.06 mmHg), $[\alpha]_D$ −29.9° (*c*=4.6, EtOH)].

tert-Butyl 2-Methylacetoacetate (**8b**): *tert*-Butyl acetoacetate (4.6 ml, 0.030 mol) was added to a suspension of sodium hydride (50% oil dispersion, 1.7 g, 0.036 mol) in 10 ml of THF at 0 °C. The reaction mixture was stirred at 0 °C for 1 h, then a solution of methyl iodide (2.2 ml, 0.036 mol) in THF (10 ml) was added. The whole was stirred at room temperature for 16 h, and then diluted with ether. The solution was washed with 10% aqueous HCl, saturated aqueous $NaHCO_3$, and saturated aqueous NaCl, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The crude product was subjected to distillation under reduced pressure to give **8b** (5.0 g, 78% yield): bp 50 °C (4 mmHg). IR ν_{max}^{film} cm^{-1}: 1745 (ester), 1725 (C=O). NMR (CCl_4) δ: 1.23 (3H, d, *J*=2 Hz, $CHC\underline{H}_3$), 1.43 (9H, s, $C(CH_3)_3$), 2.07 (3H, s, $COCH_3$), 3.20 (1H, q, *J*=7, 7 Hz, COCHCO). MS *m/z*: 172 (M^+). Exact mass determination: 172.0976 (Calcd for $C_9H_{16}O_3$: 172.1000).

Palladium-Catalyzed Asymmetric Allylations of Aldehyde- or Keto-enamines Allylating Reagents: Commercially available allyl acetate (**4a**) and allyl halides (**4h**—**j**) were used. Allyl benzoate (**4b**),[16] *p*-nitrobenzoate (**4c**),[17] and *p*-toluenesulfonate (**4f**[18]) were prepared according to the methods reported previously.

Allyl α- or β-Naphthoate (**4d** or **4e**): A solution of α- or β-naphthoic acid (1.0 g, 0.006 mol) and allyl alcohol (0.6 ml, 0.009 mol) in benzene (10 ml) was refluxed in the presence of a catalytic amount of concentrated sulfuric acid for 19 h using a Dean–Stark apparatus. After cooling, the reaction mixture was diluted with ether. The ethereal solution was washed with saturated aqueous $NaHCO_3$ and saturated aqueous NaCl, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The crude product was subjected to preparative TLC (benzene–hexane, 1 : 2) to give **4d** (0.9 g, 72% yield) or **4e** (1.1 g, 87% yield).

4d: IR ν_{max}^{film} cm^{-1}: 1700 (ester), 1670 (C=C), 1580 (aromatic). NMR (CCl_4) δ: 4.86 (2H, d, *J*=6 Hz, $C\underline{H}_2CH=CH_2$), 5.10—6.56 (3H, m, $CH_2C\underline{H}=C\underline{H}_2$), 7.16—8.33 (7H, m, $C_{10}H_7$). MS *m/z*: 212 (M^+). Exact mass determination: 212.0893 (Calcd for $C_{14}H_{12}O_2$: 212.0887).

4e: IR ν_{max}^{film} cm^{-1}: 1700 (ester), 1620 (C=C), 1580 (aromatic). NMR (CCl_4) δ: 4.80 (2H, d, *J*=6 Hz, $C\underline{H}_2CH=CH_2$), 5.13—6.56 (3H, m, $CH_2C\underline{H}=C\underline{H}_2$), 7.10—8.70 (7H, m, $C_{10}H_7$). MS *m/z*: 212 (M^+). Exact mass determination: 212.0812 (Calcd for $C_{14}H_{12}O_2$: 212.0798).

Allyl *o*-Toluenesulfonate (**4g**): *o*-Toluenesulfonyl chloride (1.0 g, 0.005 mol) was added to a solution of allyl alcohol (0.6 ml, 0.008 mol) in 10 ml of pyridine at 0 °C. The reaction mixture was stirred at 0 °C for 4 h and then diluted with ether. The solution was washed with 10% aqueous HCl, saturated aqueous $NaHCO_3$, and saturated aqueous NaCl, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The crude product was subjected to preparative TLC (ether–hexane, 1 : 2) to give **4g** (0.9 g, 86% yield). IR ν_{max}^{film} cm^{-1}: 1640 (C=C), 1600 (aromatic), 1370 (OSO_2). NMR (CCl_4) δ: 2.60 (3H, s, $C_6H_4C\underline{H}_3$), 4.43 (2H, d, *J*=6 Hz, $C\underline{H}_2CH=CH_2$), 5.00—6.50 (3H, m, $CH_2C\underline{H}=C\underline{H}_2$), 6.90—8.06 (4H, m, C_6H_4). MS *m/z*: 212 (M^+). Exact mass determination: 212.0502 (Calcd for $C_{10}H_{12}O_3S$: 212.0506).

Genaral Procedures: A solution of (*S*)-**1** (50 mg, 0.197 mmol) and an aldehyde (2-phenylpropional (**2a**), 3-(*p*-*tert*-butylphenyl)isobutanal (**2b**), or 2-methylbutanal (**2c**)) or a ketone (cyclohexanone or ethyl or *tert*-butyl 2-methylacetoacetate (**8a**[13] and **8b**)) (0.197 mmol) in 10 ml of benzene was refluxed for 4 h using a Dean–Stark apparatus. The solution was concentrated *in vacuo* to give the aldehyde- or keto-enamine ((*S*)-**3a**—**c**, (*S*)-**6**, or (*S*)-**8a**, **b**).

A dry 25 ml two-necked flask equipped with a septum inlet and magnetic stirring bar, and containing tetrakis(triphenylphosphine)palladium (46 mg, 0.039 mmol) or bis(dibenzylideneacetone)palladium (23 mg, 0.039 mmol) was flushed with nitrogen, and maintained under a positive pressure of nitrogen. A solution of an enamine (0.197 mmol) obtained above in 6 ml of THF was added to the above flask and the mixture was stirred at room temperature for 1 h and then a solution of an allylating reagent (**4a**—**j**) (2.0 eq) in 4 ml of THF was added. The whole was stirred at the temperature for the time shown in Tables I and II. The reaction mixture was treated with 10% aqueous HCl–benzene under reflux for 1 h (for **5a**—**c**) or with AcONa–AcOH–H_2O–benzene at room temperature for 1 h (for **7** and **10a**, **b**). The reaction mixture was diluted with ether. The ethereal solution was washed with 10% aqueous HCl, saturated aqueous $NaHCO_3$, and saturated aqueous NaCl, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The crude product was subjected to preparative TLC to give the corresponding α-allyl carbonyl compound: (*R*)-(−)-2-methyl-2-allyl-4-pentenal (**5a**) (benzene–hexane, 1 : 2),[8b,19] (*R*)-(+)-2-(*p*-*tert*-butylphenyl)methyl-2-methyl-4-pentenal (**5b**) (isopropyl ether–hexane, 1 : 3), (*S*)-(−)-2-ethyl-2-methyl-4-pentenal (**5c**), (isopropyl ether–hexane, 1 : 5),[20] (*S*)-(−)-2-allylcyclohexanone (**7**) (ether–hexane, 1 : 5),[8a,11] ethyl or *tert*-butyl (*S*)-(−)-2-allyl-2-methylacetoacetate (**10a**) (ether–hexane, 1 : 5)[14] or (**10b**) (ether–hexane, 1 : 3).[19] The yields, optical rotations, and the enantiomeric excess of the products are summarized in Tables I and II.

(*R*)-(−)-**5b**: IR ν_{max}^{film} cm^{-1}: 1730 (ester), 1645 (C=C), 1600 (aromatic). NMR (CCl_4) δ: 1.00 (3H, s, CH_3), 1.30 (9H, s, $C(CH_3)_3$), 1.86—2.36 (2H, m, $C\underline{H}_2C_6H_4$), 2.70 (2H, d, *J*=2 Hz, $C\underline{H}_2CH=CH_2$), 4.70—6.16 (3H, m, $CH_2C\underline{H}=C\underline{H}_2$), 6.70—7.43 (4H, m, C_6H_4), 9.46 (1H, s, CHO). MS *m/z*: 244 (M^+). Exact mass determination: 244.1834 (Calcd for $C_{17}H_{24}O$: 244.1827).

Conversion of (*S*)-(−)-10a,b into (*S*)-(−)-2-Acetyl-2-methyl-4-pentenyl Benzoate (*S*)-(−)-2-Acetyl-2-methyl-4-pentenyl Benzoate: Lithium aluminum hydride (22 mg, 0.578 mmol) was added to a solution of (*S*)-(−)-**10a** (90 mg, 0.489 mmol, $[\alpha]_D^{21}$ −13.5° (*c*=1.35, $CHCl_3$), 45% ee) in 10 ml of ether cooled to 0 °C. The reaction mixture was stirred at 0 °C for 1 h and then quenched with H_2O (0.1 ml) and 10% aqueous NaOH (0.06 ml). The mixture was diluted with ether and then refluxed for 1 h. The precipitates were filtered and washed with ether. The filtrates were combined and concentrated *in vacuo* to give 2-allyl-2-methyl-1,3-butanediol (70 mg) [IR ν_{max}^{film} cm^{-1}: 3300 (OH)].

Pyridine (77 mg, 0.978 mmol) and benzoyl chloride (83 mg, 0.586 mmol) were added to a solution of 2-allyl-2-methyl-1,3-butanediol obtained above in 10 ml of THF at 0 °C. The reaction mixture was stirred at 0 °C for 3 h and then diluted with ether. The solution was washed with 10% aqueous HCl, saturated aqueous $NaHCO_3$, and saturated aqueous NaCl, dried over anhydrous Na_2SO_4, and concentrated *in vacuo* to give 2-(1-hydroxyethyl)-2-methyl-4-pentenyl benzoate (121 mg) [IR ν_{max}^{film} cm^{-1}: 3300 (OH), 1740 (ester), 1580 (aromatic)].

The Jones reagent (0.5 ml) was added to a solution of the benzoate obtaine above in 2 ml of acetone at 0 °C. The reaction mixture was stirred at 0°C for 10 min and then quenched with isopropyl alcohol. The reaction mixture was concentrated *in vacuo*, and ether was added to the residue. The suspension was washed with saturated aqueous $NaHCO_3$ and saturated aqueous NaCl, and dried over anhydrous Na_2SO_4. The solution was concentrated *in vacuo*, and the crude product was subjected to preparative TLC (ether–hexane, 2 : 1) to give (*S*)-(−)-2-acetyl-2-methyl-4-pentenyl benzoate (118 mg, 98% yield), $[\alpha]_D^{21}$ −7.6° (*c*=2.5, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 1745 (ester), 1725 (C=O). NMR (CCl_4) δ: 1.13 (3H, s, CH_3), 1.20—1.53 (2H, m, $C\underline{H}_2CH=CH_2$), 2.32 (3H, s, $COCH_3$), 4.23 (2H, d, *J*=2 Hz, OCH_2), 4.68—5.35 (3H, m, $CH_2C\underline{H}=C\underline{H}_2$), 7.20—8.10 (5H, m, C_6H_5). MS *m/z*: 246 (M^+). Exact mass determination: 246.1371 (Calcd for $C_{15}H_{18}O_3$: 246.1360).

Treatment of (−)-**10b** (90 mg, 0.425 mmol, $[\alpha]_D^{24}$ −14.8° (*c*=1.6, $CHCl_3$)) under the same conditions led to (*S*)-(−)-2-acetyl-2-methyl-4-pentenyl benzoate (116 mg, 97% yield, $[\alpha]_D^{20}$ −10.9° (*c*=2,2, $CHCl_3$)).

On the basis of the above results, the optical rotation of cptically pure (*S*)-(−)-**10b** was calculated to be $[\alpha]_D$ −22.7°C ($CHCl_3$).

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