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Novel C_2-Symmetric Diphosphine Ligand with only the Planar Chirality of Ferrocene

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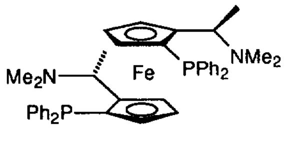
Abstract: The first C_2-symmetric diphosphine ligand possessing only the planar chirality of ferrocene was prepared from 1,1'-bis(diphenylphosphino)-2,2'-bis(oxazolinyl)ferrocene by the transformation of the oxazoline moieties in the molecule and with this new chiral ferrocene diphosphine ligand, up to 92% ee was obtained for the palladium-catalyzed allylic alkylation of 1,3-diphenyl-2-propenyl acetate with 2,4-pentanedione. Copyright © 1996 Elsevier Science Ltd

The design and the preparation of chiral diphosphine ligands, particularly with C_2-symmetry, are of great importance in the development of transition metal-catalyzed enantioselective reactions.[1] Meanwhile, the planar chiralities of ferrocene, which were found to provide excellent chiral environments, have received intensive attention.[2] Moreover, a C_2-symmetric ferrocene diphosphine ligand **1** with both tetrahedral and planar elements of chirality has shown highly asymmetric induction ability.[3] However, only limited study on this kind of ligand has been carried out due to the difficulty of synthesis. We recently reported a simple preparation of novel C_2-symmetric ferrocene diphosphine ligands, (-)-(*S*)-(*S*)-1,1'-bis(diphenylphosphino)-2,2'-bis[(*S*)-4-substituted oxazolin-2-yl)ferrocenes (**2**) *via* the highly diastereoselective ortho-lithiation of the corresponding 1,1'-bis[(*S*)-4-substituted oxazolin-2-yl]ferrocenes.[4] However, these diphosphine compounds did not give the expected 1:1 P,P-chelate with palladium(II), but a C_2-symmetric 1:2 P,N-chelate was formed upon using 2 equiv. of dichlorobis(acetonitrile)palladium(II) due to the function of the oxazoline groups.[5] In this paper, we wish to report the preparation of a new C_2-symmetric diphosphine ligand with only the planar chirality of ferrocene, (-)-(*S*)-(*S*)-1,1'-bis(diphenylphosphino)-2,2'-bis(methoxycarbonyl)ferrocene (**3**), by the transformation of the oxazoline moieties in the compound **2** and its application to palladium-catalyzed allylic alkylation.



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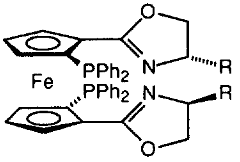

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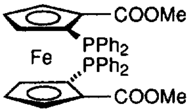
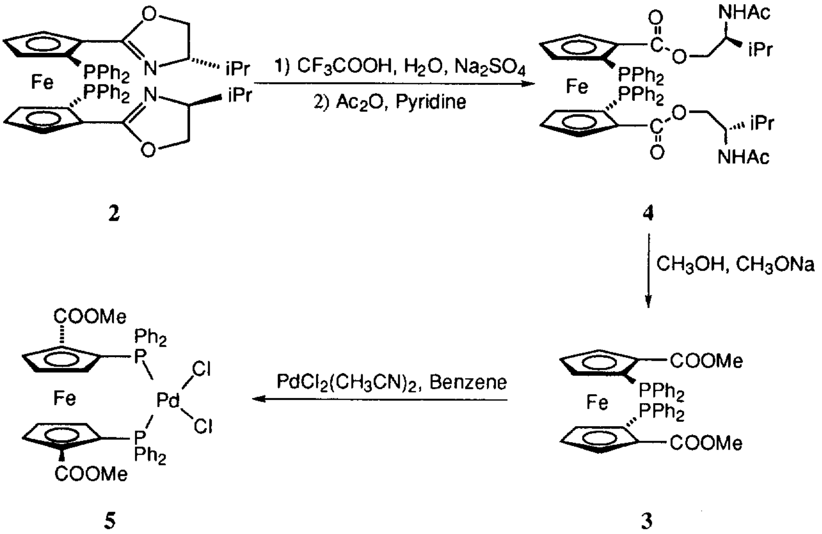


3

The compound **3** can be easily prepared from **2** by Meyer's method (Scheme 1).[6] Thus, treatment of **2** with trifluoroacetic acid in aqueous THF caused ring opening of the oxazoline to give an unstable ammonium salt. This ammonium salt was acetylated, without isolation, with acetic anhydride in the presence of pyridine to provide diester amide **4** in 61% yield.[7] Transesterification of **4** using methanolic sodium methoxide at room temperature for one day gave the compound **3** in 74% yield.[8]

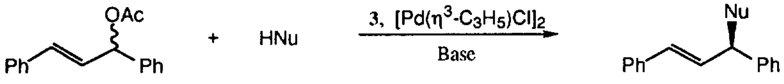


Scheme 1

Upon mixing this new diphosphine ligand **3** with 1 equiv. of dichlorobis(acetonitrile)palladium(II) in acetonitrile-d^3, the formation of only one C_2-symmetric 1:1 P,P-chelate **5** was found in ^{1}H-NMR. Treating **3** with 1 equiv. of dichlorobis(acetonitrile)palladium(II) in benzene for 1 hour followed by filtration gave **5** as a yellow solid in 97% yield (Scheme 1). Recrystallization of **5** from dichloromethane / hexane provided orange single crystals,[9] which contain one molecule of dichloromethane per one complex as determined by ^{1}H-NMR and elementary analysis.

Palladium-catalyzed allylic alkylation, particularly the 1,3-diphenylallylic alkylation, has received considerable attention[10] and excellent enantioselectivities have been documented with N,N-chelating and P,N-chelating ligands.[11] However, only few P,P-chelating ligands, especially with C_2-symmetry, gave excellent results for the 1,3-diphenylallylic alkylation.[12] With this new C_2-symmetric P,P-chelating ligand **3** in hand, we first carried out this reaction as a preliminary experiment and the result is shown in Scheme 2 and Table 1.

From Table 1 it is seen that ligand **3** shows excellent properties for the allylic alkylation of 1,3-diphenyl-2-propenyl acetate with dimethyl malonate. It is reported that in many cases the base used in this reaction has a significant effect on enantioselectivity.[10c] However, in our case, there is no great difference between NaH and *N,O*-bis(trimethylsilyl)acetamide (BSA) used as the base, and both of them gave high enantioselectivities for the allylic alkylation of 1,3-diphenyl-2-propenyl acetate with dimethyl malonate. The reaction temperature has considerable influence on the reaction rate. At room temperature, the reaction proceeded fast and completed within 1 hour with both NaH and BSA as base. Lowering the temperature decreased the reaction rate and when the temperature was at -25 °C, the reaction was very slow and only 45% yield was obtained after 72 hours. The reaction temperature has some influence on enantioselectivity also, and from Table 1 it is seen that the best reaction temperature was 0 °C, at which temperature up to 90% ee was obtained for the product **7a**. Changing the nucleophile to 2,4-pentanedione also gave excellent enantioselectivity and up to 92% ee was obtained for the product **7b**. This is one of the best results reported so far for the allylic alkylation of 1,3-dipheny-2-propenyl acetate with C_2-symmetric P,P-chelating ligands.[13] On using THF as the solvent instead of dichloromethane, the obtained result was unsatisfactory due to the poor solubility of the catalyst prepared from ligand **3** and $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ in THF.



6 **7a,b**

Scheme 2 (**a**: Nu = $HC(CO_2Me)_2$; **b**: Nu = $HC(COMe)_2$)

Table 1. Palladium-catalyzed allylic alkylation of 1,3-diphenyl-2-propenyl acetate[a]

HNu	Base	T (°C)	Time (h)	Product	Yield (%)	ee (%)[c]	Enantiomer[d]
$H_2C(CO_2Me)_2$	NaH	25	1	7a	91	84	(S)-(-)
$H_2C(CO_2Me)_2$	BSA-KOAc[b]	25	1	7a	96	86	(S)-(-)
$H_2C(CO_2Me)_2$	BSA-KOAc[b]	0	7	7a	94	90	(S)-(-)
$H_2C(CO_2Me)_2$	BSA-KOAc[b]	-25	72	7a	45	88	(S)-(-)
$H_2C(COMe)_2$	BSA-KOAc[b]	0	8	7b	95	92	(S)-(+)

a) Reactions were conducted with 1 mmol **6**, 3 mmol nucleophile and 3 mmol base in 3 ml of dichloromethane under argon in the presence of the catalyst which was prepared by treating 30 μmol **3** and 12.5 μmol $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ in 1 ml of dichloromethane for 1 hour before use. b) Where 20 μmol KOAc was added. c) The enantiomeric excess was determined by ^{1}H-NMR in the presence of shift reagent $Eu(hfc)_3$.[12a] d) The absolute stereochemistry of the product was determined by comparison of the optical rotation with literature values.[12a]

In summary, we have prepared the first C_2-symmetric diphosphine ligand **3** possessing only the planar chirality of ferrocene from 1,1'-bis(diphenylphosphino)-2,2'-bis(oxazolinyl)ferrocene **2** by the transformation of the oxazoline moieties in the molecule. With this new C_2-symmetric chiral diphosphine ligand, the palladium-catalyzed allylic alkylation of 1,3-diphenyl-2-propenyl acetate was carried out as a preliminary experiment and up to 92% ee was obtained for the product **7b**. The potential of this diphosphine ligand and its derivatives in other asymmetric reactions is being investigated in our laboratory.

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7 **4**: mp 102-104 °C. ^{1}H-NMR (600 MHz, $CDCl_3$) δ 7.29 (8H, m, ArH), 7.22 (8H, m, ArH), 7.12 (8H, m, ArH), 6.59 (2H, d, *J* 8.8 Hz, NH), 5.06 (2H, brs, FcH), 4.66 (2H, brs, FcH), 4.41 (2H, dd, *J* 2.6, 11.5 Hz, OCH), 4.13 (2H, m, NCH), 3.95 (2H, dd, *J* 7.3, 11.5 Hz, OCH), 3.45 (2H, brs, FcH), 2.08 (2H, m, Me_2CH), 1.88 (6H, s, $COCH_3$), 1.07 (6H, d, *J* 6.5 Hz, CH_3), 1.02 (6H, d, *J* 6.5 Hz, CH_3). IR (KBr) 2962, 1714, 1658, 1529, 1434, 1371, 1319, 1253, 1153, 1070, 838 cm^{-1}. FAB-MS (m/z) 897.

8 **3**: mp 198 °C (decomposed). $[\alpha]_D^{25}$ = -595.2 (c 0.25, $CHCl_3$). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.31-7.14 (20H, m, ArH), 5.09 (2H, brs, FcH), 4.56 (2H, t, *J* 2.7 Hz, FcH), 3.74 (6H, s, CH_3), 3.48 (2H, brs, FcH). ^{31}P-NMR($CDCl_3$, $P(OCH_3)_3$) δ -160.28. IR (KBr) 2946, 1707, 1477, 1448, 1317, 1273, 1195, 1147, 1066, 746 cm^{-1}. FAB-MS (m/z) 670. Anal. Calcd. for $C_{38}H_{32}O_4P_2Fe$: C, 67.91; H, 4.95. Found: C, 68.08; H, 4.81.

9 **5** · CH_2Cl_2: mp 236 °C (decomposed). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.25 (4H, m, ArH), 8.11 (4H, m, ArH), 7.40 (12H, m, ArH), 5.30 (2H, s, Cl_2CH_2), 4.81 (2H, brs, FcH), 4.49 (2H, t, *J* 2.7 Hz, FcH), 4.29 (2H, brs, FcH), 3.35 (6H, s, OCH_3). ^{31}P-NMR($CDCl_3$, $P(OCH_3)_3$) δ -95.69. IR (KBr): 2947, 1720, 1481, 1448, 1373, 1330, 1265, 1194, 1163, 1092, 999, 746 cm^{-1}. FAB-MS (m/z) 848. Anal. Calcd. for $C_{39}H_{34}O_4P_2FePdCl_4$: C, 50.22; H,3.67. Found: C, 50.08; H, 3.63.

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13 It was reported that 90% ee for **7a** and **7b** was obtained using Chiraphos[12b] and BINAP[12b,c] as the chiral ligand, respectively.

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