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TETRAHEDRON: *ASYMMETRY*

A new aminophosphine ligand containing axial and planar chiral elements

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Abstract

Synthesis and X-ray structure analyses of the chiral aminophosphine ligand **2a**, accessible *via* diastereoselective *ortho*-lithiation of aminoferrocene **5**, and of its cationic 1,3-diphenyl-π-allyl palladium complex **6** are reported. Its application in asymmetric allylic alkylation reactions showed asymmetric inductions of up to 71%. © 1998 Elsevier Science Ltd. All rights reserved.

During the last decades an impressive number of chiral auxiliaries have been reported.[1] This booming synthetic activity was drawn mainly by the intention to optimize selectivity and reactivity of asymmetric catalytic conversions with respect to the appropriate adjustment of the ligand geometry to the reaction type (and mechanism) and substrate structure. Among these, the group of ferrocene based ligands is somewhat outstanding since most combine (at least) one element of central chirality with planar chirality arising from the non-symmetrical disubstitution of one cyclopentadienyl ring.[2]

To extend our previous work on 2,2′-bridged binaphthyl ligands like **1**[3] we were interested in the synthesis of further ligands with different types of P–N linkages such as **2a** or **2b**, not only changing the bite-angle but also introducing different degrees of steric interaction above and below the basal plane of the substrate complex.

A synthesis of **2a** in four steps from ferrocene is outlined in Scheme 1. To obtain the key intermediate **5** a more convenient access to aminomethylferrocene **4**[4] was desired. We found that **4** can be prepared directly from the methiodide of Mannich base **3**[5] when heating in a mixture of aqueous ammonia/benzene for 48 h in an autoclave (80%). The primary amine **4** was cyclized with (*S*)-2,2′-bis(bromomethyl)-1,1′-binaphthyl[6] under standard conditions to afford **5** (79%) which was finally treated with s-BuLi/Et_2O followed by reaction with chlorodiphenylphosphine to give predominantly aminophosphine **2a** (65%).[7,12] *ortho*-Lithiation under various conditions did not alter the diastereoselectivity significantly which was

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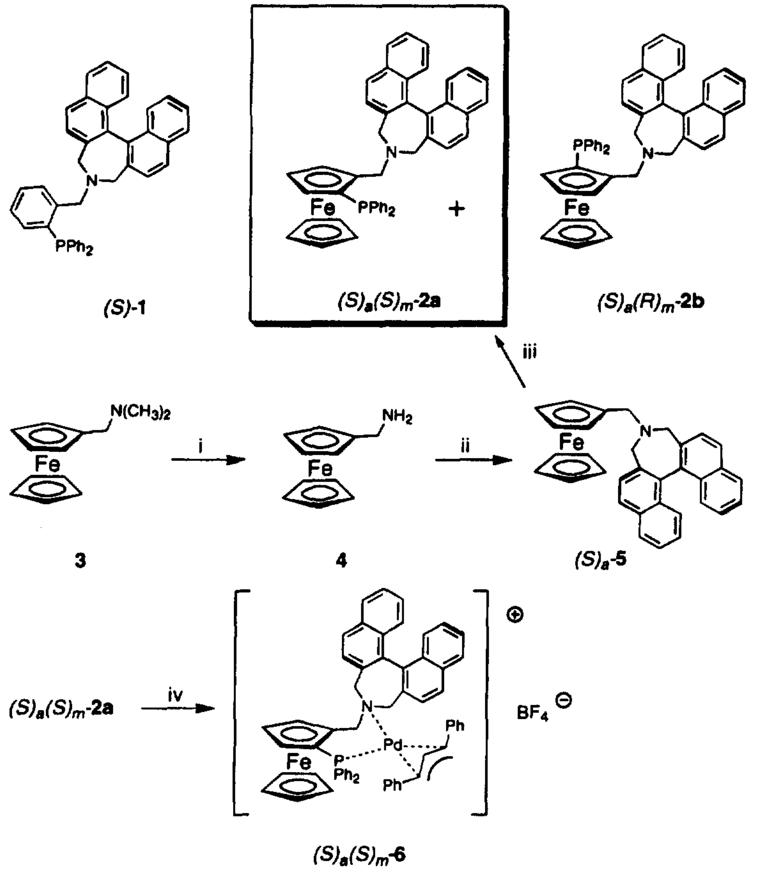
found to be 9:1, independently of solvent, temperature and lithiation reagent used. The relative configuration of **2a** was deduced from an X-ray structure analysis[7,12] of the optically active ligand, revealing an $(S)_a(S)_m$-configuration for the predominant product of the *ortho*-lithiation of $(S)_a$-**5** (Fig. 1).[8]



Reagents: i, MeI, conc. ammonia / benzene 100 °C, 48 h, 80%; ii, (*S*)-2,2'-bis(bromomethyl)-1,1'-binaphthyl, triethylamine, benzene, reflux, 18 h, 79%; iii, (a) s-BuLi, ether, room temp. 4 h, (b) chlorodiphenylphosphine, -78 °C→room temp., 65%; iv, 1,3-diphenyl-π-allyl-palladium acetate dimer, $AgBF_4$, CH_2Cl_2/aceton, 81%.

Scheme 1.

A preliminary study to test the efficiency of **2a** in the palladium catalyzed allylic alkylation reactions[9] revealed improved asymmetric induction for cyclic substrates and pent-3-en-2-yl acetate but a sharp drop in the enantioselectivity for 1,3-diphenyl-2-propen-1-yl acetate compared with **1** (Table 1). We speculate that the moderate selectivities are due to steric strain in the chelate ring which facilitates at least temporary cleavage of the Pd–N bond during the catalytic cycle. Evidence was found in the X-ray structure of the palladium–π-allyl complex **6** (Fig. 2) which showed an unusually large N–C(11)–C(6) angle of 120° and also a distortion of one P–Ph ring which is directly opposed to one allyl–Ph (C(7)–P–C(40), 101°, Pd–P–C(40), 118°).[10] This lability is also reflected in the appearance of a C_2-symmetrical binaphthyl fragment in the ^1H NMR spectrum of the Pd–π-allyl complex indicating low thermodynamic and/or kinetic stabiliy of the Pd–N bond.

A more detailed mechanistic investigation, a synthetic approach to **2b** and the extension of the *ortho*-lithiation/E^+ protocol to the preparation to other chiral aminoferrocene ligands are presently in progress.

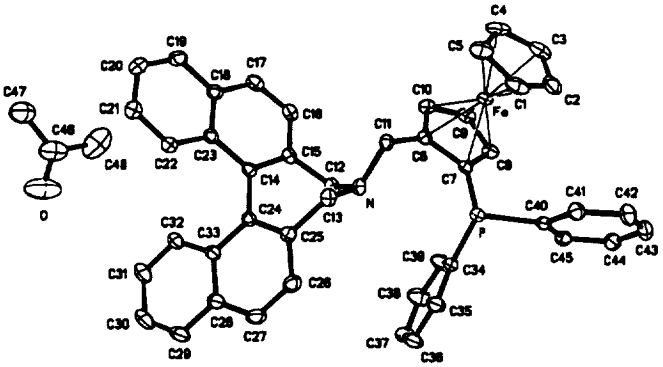
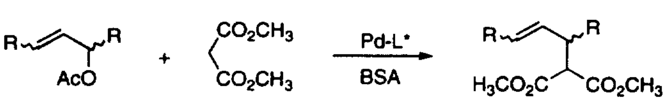


Fig. 1. Molecular representation of $(S)_a(S)_m$-N-(2-diphenylphosphino-1-ferrocenylmethyl)-3,5-dihydro-4*H*-dinaphth[2,1-c:1′,2′-e] azepine (**2a**) (acetone solvate)[7]

Table 1
Palladium catalyzed allylic alkylation reactions[a]



entry	ligand config. / substrate	% e.e.[b] (config. of prod) *isol.yield* $(S)_a(S)_m$-**2a**	$(S)_a$-**1**
1	1,3-diphenyl-2-propen-1-yl acetate	44 (*S*) *79*	**97 (*S*)** *95*[3b]
2	3-penten-2-yl acetate	**37 (+)** *73*	5 (+) *80*[3b]
3	2-cyclopenten-1-yl acetate	**71 (*R*)** *64*	15 (*R*) *63*[3c]
4	2-cyclohexen-1-yl acetate	**36 (*R*)** *23*	28 (*R*) *86*[3b]
5	2-cyclohepten-1-yl acetate	56 (*R*) *82*	**63 (*R*)** *74*[3c]

[a] Reactions were conducted on a 1 mmol scale with N,O-bis(trimethylsilyl)acetamide (BSA) in CH_2Cl_2, 0.5 mol% of $[Pd(\pi\text{-}C_3H_5)Cl]_2$ and 2 mol% of ligand at room temp.; for experimental details see [11a]. [b] E.e.'s were determined by HPLC (entry 1) [11a], GC (entry 2) [11a] or on the basis of highest specific rotations reported (entries 3-5). [11b]

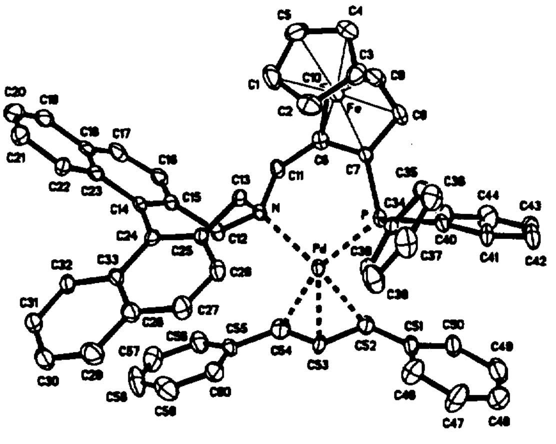


Fig. 2. Molecular representation of the predominantly formed 1,3-diphenyl-π-allyl palladium complex **6** prepared from $(S^*)_a(S^*)_m$-**2a** as encountered in the crystalline tetrafluoroborate methanol solvate[10]

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6. (−)-(*S*)-2,2′-Bis(bromomethyl)-1,1′-binaphthyl: $[\alpha]_D^{20}$ −165 (c=1.00, benzene), see Maigrot, N.; Mazaleyrat, J.-P. *Synthesis* **1985**, 317.
7. Selected data for: (±)-**2a**: orange–red crystals from acetone; mp: 222–225°C (dec.). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.66 (2H, bd, J=12.0 Hz); 3.44 (1H, bd, J≈13.7 Hz); 3.45 (2H, d, J=12.0 Hz); 3.76 (1H, dd, J=13.7, 1.5 Hz); 3.80 (1H, bs); 4.03 (5H, s); 4.32 (1H, pt, J=2.5 Hz); 4.65 (1H, bs); 6.87 (3H, m); 7.14 (2H, m); 7.22 (2H, m); 7.32 (2H, d, J=7.9 Hz); 7.34–7.44 (7H, m); 7.58 (2H, m); 7.85 (2H, d, J=8.4 Hz); 7.92 (2H, d, J=8.4 Hz). $^{31}P\{^1H\}$ NMR (162 MHz) δ: −21.89 (s). MS (FD) m/z: 677.5 (100%, M^+). Analysis calc. for $C_{45}H_{36}FeNP$: C 79.77; H 5.35; N 2.07; P 4.57; Fe 8.24; found: C 79.54; H 5.61; N 1.93; P 4.81. $(S)_a(S)_m$-**2a**: mp: 136–140°C. $[\alpha]_D^{20}$ −31.7 (c=0.7, CH_2Cl_2). Crystal data for $(S)_a(S)_m$-**2a** (acetone solvate): $C_{48}H_{42}FeNOP$, M=735.65, monoclinic, space group $P2_1$, a=9.566(3), b=11.531(4), c=17.634(6) Å, α=90°, β=96.10(2)°, γ=90°, U=1934.1(11) Å^3, Z=2, D_c=1.263 Mg/m^3, T=300(2) K, μ=0.47 mm^{-1}, $F(000)$=772, orange prism (0.46×0.30×0.30 mm). Data were collected on a Siemens SMART 3-circle with a CCD area detector. Structure solution by the Patterson method, refinement by full-matrix least-squares on F^2 (SHELX-97), Ref. 12. Data/restraints/parameters=10950/1/470; final $R1$=0.0449, $wR2$=0.0779 (all data). CCDC 182/102876.
8. The indices ‘a’ and ‘m’ denote ‘axial’ and ‘metallocene’ chirality.
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10. Crystal data for the racemic palladium complex $(S^*)_a(S^*)_m$-**6** in the form of its tetrafluoroborate methanol solvate: $C_{61}H_{53}BF_4FeNOPPd$, M=1096.07, monoclinic, space group $P2_1/c$, a=13.274(6), b=21.590(10), c=18.501(8) Å, α=90°, β=107.03(2)°, γ=90°, U=5070(4) Å^3, Z=4, D_c=1.436 Mg/m^3, T=299(2) K, μ=0.73 mm^{-1}, $F(000)$=2248, orange prism (0.2×0.1×0.1 mm). Data were collected on a Siemens SMART 3-circle diffractometer (see above). Structure solution by direct methods, refinement by full-matrix least-squares on F^2, data/restraints/parameters=6517/0/641; final $R1$=0.117, $wR2$=0.157 (all data). CCDC 182/102877.
11. (a) For typical procedures see: Widhalm, M.; Wimmer, P.; Klintschar, G. *J. Organomet. Chem.* **1996**, *523*, 167. (b) For a compilation of specific rotations see: Sennhenn, P.; Gabler, B.; Helmchen, G. *Tetrahedron Lett.* **1994**, *35*, 8595.
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