Atropisomerism and Helicity

Helical Chirality Control of Palladium Complexes That Bear a Tetrakis(phosphanyl)terphenyl Ligand: Application as Asymmetric Lewis Acid Catalysts**

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Helical structures (e.g. classical helicenes[1]) have attracted much attention for quite some time. The helical chirality stems from the nonplanar structure and, therefore, we designed the novel 2,4′,6′,2″-tetrakis(diphenylphosphanyl)-[1,1′;3′,1″]terphenyl (tetraphos) ligand model, which exhibits nonplanar helicity when complexed to metal centers (Scheme 1).

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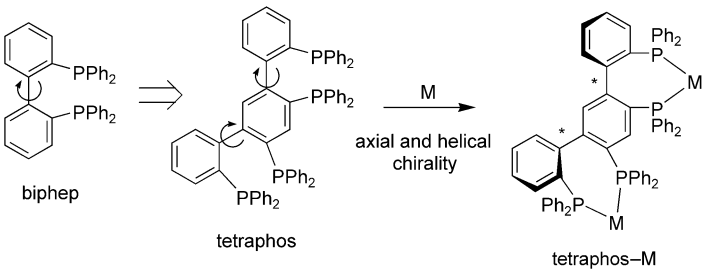


Scheme 1. *Tropos* nature of the tetraphos–M complex.

Many chiral phosphane ligands have been reported to induce high enantioselectivity in catalytic asymmetric reactions,[2] and much attention has been devoted to their syntheses. However, the synthesis and resolution of these chiral P ligands are difficult because of racemization at higher temperature.[3] We have reported the chirally flexible (*tropos*, meaning turn in Greek) biphep ligand, which has a biphenyl backbone[4] whose axial chirality can be controlled by chiral controllers without resolution. Herein we report a further advanced strategy that employs the *tropos* nature of the designed tetraphos ligand to generate helicity upon complexation with a metal and its application as an asymmetric Lewis acid catalyst.

The tetraphos–Pd complex was quantitatively obtained from the tetraphos ligand and 2 equivalents of $[PdCl_2(cod)]$ (cod = cycloocta-1,5-diene) in CH_2Cl_2. Recrystallization from CH_2Cl_2/MeOH gave single crystals, which allowed the 3D structure of this complex to be clarified by X-ray crystallographic analysis (Figure 1a).[5] The complex has two biphep–Pd units in which the phenyl groups adopt either axial or equatorial orientations (Figure 1b). The biphep portions of the tetraphos–Pd complex are quite similar not only to the biphep–Pd complex but also to many binap–metal complexes.[4d,6] In Figure 1, the axial chirality is *S,S* and the helical chirality is *P* (plus), that is, clockwise around the helix axis. The *meso* diastereomer complex, which would have *S,R* axial chirality, was not obtained, apparently as a consequence of the sterically demanding diphenylphosphane groups. Once the axial chirality (*S* or *R*) is determined in one biphenyl unit, the axial and helical chirality in the other unit is inevitably fixed as *S,P* or *R,M*, respectively.

3,3′-Dimethyl-2,2′-diamino-1,1′-binaphthyl (dm-dabn) with sterically demanding methyl substituents in the 3,3′-positions of 2,2′-diamino-1,1′-binaphthyl (dabn)[4b,7] was used for the enantiomeric resolution and isomerization of the tetraphos–Pd complex (±)-**1** complex (Scheme 2). Complex (±)-**1** was treated with 2 equivalents of (*S*)-dm-dabn to give the single diastereomer (*P,S,S*)-**2**, along with remaining (*M,R,R*)-**1** and (*S*)-dm-dabn. Importantly, no isomerization of the remaining (*M,R,R*)-**1** to (*P,S,S*)-**1** was observed to complex with (*S*)-dm-dabn at room temperature for more than 120 h. After heating at 80 °C for 12 h, however, only (*P,S,S*)-**2** was obtained through isomerization of (*M,R,R*)-**1**.[8]

Under the same conditions, the combination of biphep–Pd complex (±)-**3** and 1 equivalent of (*S*)-dm-dabn gave the single diastereomer (*S*)-**4** through isomerization of (*R*)-**3** at

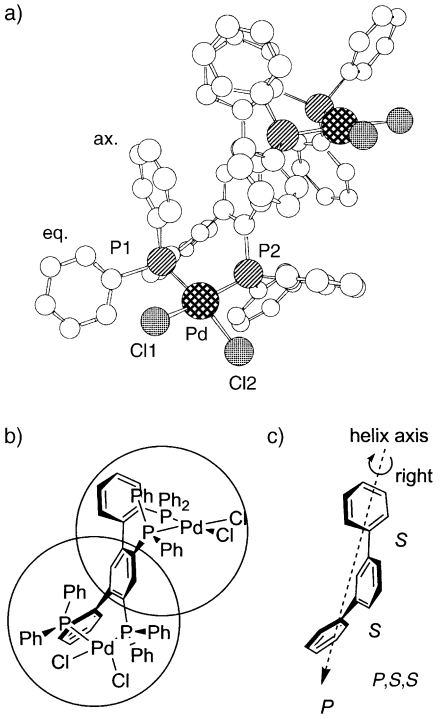


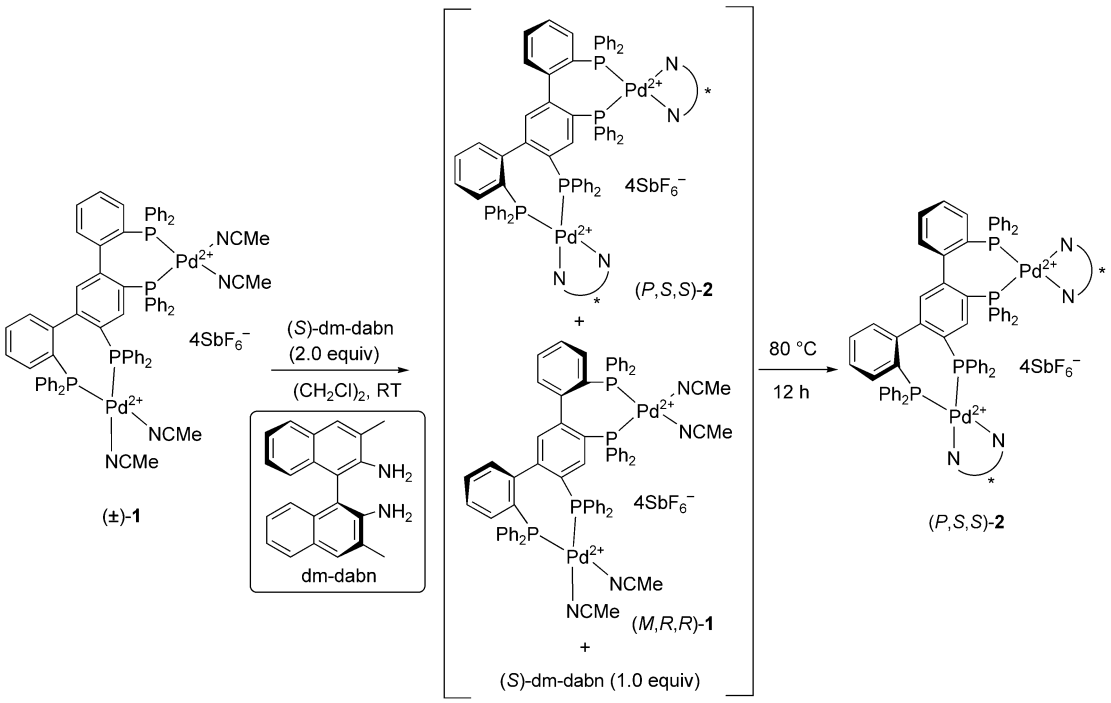
Figure 1. a) X-ray crystal structure of the tetraphos–Pd complex. Selected bond lengths [Å]: Pd-P1 2.241(2), Pd-P2 2.261(2), Pd-Cl1 2.369(3), Pd-Cl2 2.347(2), selected bond angles [°]: P1-Pd-P2 93.67(3), Cl1-Pd-Cl2 91.42(4). b) tetraphos–Pd complex with two biphep units c) Helical chirality of the tetraphos–Pd complex.

80 °C within a shorter period of time (Scheme 3).[4d] It was therefore clear that tetraphos–Pd complex **1** changes its conformation much less readily than biphep–Pd complex **3**.

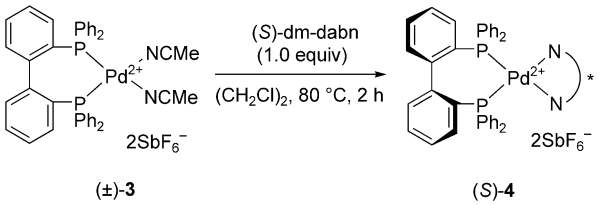
Next, complexation of (±)-**1** and 2 equivalents of (*S*)-dabn also gave a diastereomeric mixture in a nonselective manner ((*P,S,S*)-**5**/(*M,R,R*)-**5** = 1:1) (Scheme 4).[9] However, the diastereomeric mixture was converted into the single diastereomer, even at room temperature for 120 h (or 80 °C for 2 h). While the configuration of **1** was retained at room temperature as shown in Scheme 2, the dabn complex **5** isomerized under the same conditions. Therefore, the flexibility of tetraphos–Pd complex **1** can be increased by association of the chiral controller dabn.

In the combination of biphep–Pd complex (±)-**3** and 1 equivalent of (*S*)-dabn, isomerization of (*R*)-**6** took place at 80 °C for 8 h to give the single *S* diastereomer, but not at room temperature (Scheme 5).[4e] It can therefore be seen that tetraphos–Pd complex **1** is more rigid than biphep–Pd complex **3** by itself, but more flexible with a chiral diamine controller.

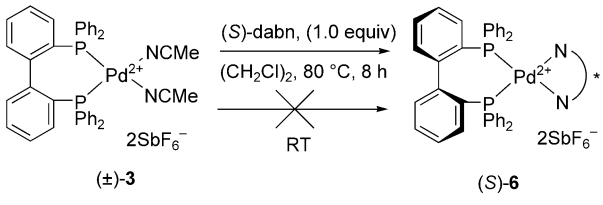
These enantiopure tetraphos–Pd complexes obtained through isomerization by diamines were employed as asymmetric catalysts for carbon–carbon bond-forming reactions. As a probe reaction, the carbonyl-ene reaction of methylenecyclohexane (**7**) and ethyl glyoxylate (**8**) was examined (Table 1).[2a,10] Enantiopure [(*S*)-binap–Pd–(*S*)-dabn] resulted in moderate enantioselectivity and yield (Table 1, entry 1). The [biphep–Pd–dabn] complex led to a decrease in enantio-



Scheme 2. Chirally stable tetraphos–Pd complex at room temperature and its isomerization to the diastereopure form at 80 °C.



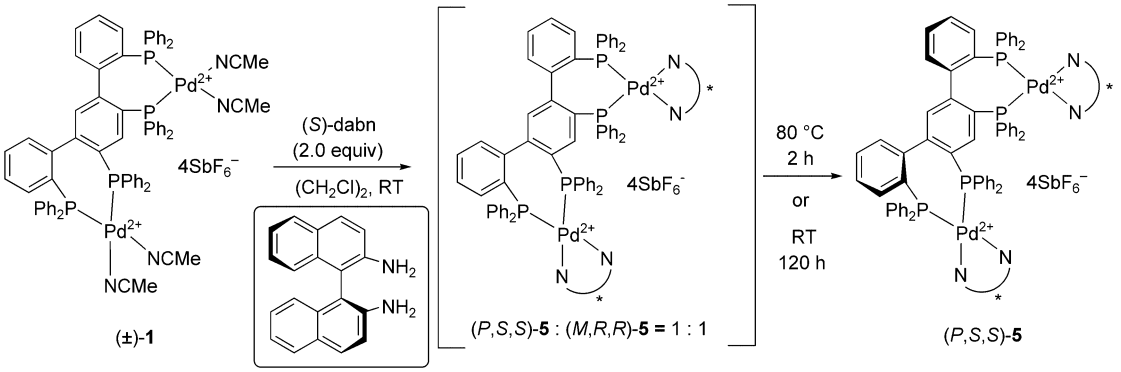
Scheme 3. Isomerization of the biphep–Pd complex by (*S*)-dm-dabn.



Scheme 5. Isomerization of the biphep–Pd complex by (*S*)-dabn.

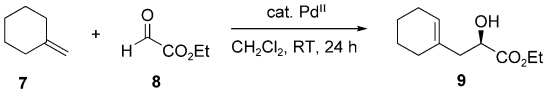
selectivity (Table 1, entry 2). However, a higher yield and enantioselectivity was observed with [tetraphos–Pd–dabn] ((*P,S,S*)-**5**) than with [biphep–Pd–dabn] ((*S*)-**6**) and [(*S*)-binap–Pd–(*S*)-dabn] (Table 1, entry 3). These results unambiguously prove the efficiency of *tropos* but sterically demanding and hence relatively rigid helical tetraphos ligands. The complex (*P,S,S*)-**2**, which bears dm-dabn, gave a slightly lower enantioselectivity (Table 1, entry 4).

In summary, we have succeeded in control over not only axial but also helical chirality of Pd complexes that bear the *tropos* tetraphos ligand. Significantly, the flexibility of the tetraphos–Pd complex can be increased by association of the chiral controller dabn. The tetraphos–Pd complexes, through isomerization into single enantiomers, lead to a higher enantioselectivity and yield, as integrated asymmetric catalysts for the carbon–carbon bond-forming reaction.



Scheme 4. Isomerization of the [tetraphos–Pd–dabn] complex in diastereopure form at room temperature.

Table 1: Asymmetric carbonyl-ene reaction by Pd catalysts with chirally flexible phosphane ligands.



7 8 9

Entry	Pd^{II} catalyst[a]	[mol%]	*ee* [%][b]	Yield [%][c]
1	[(*S*)-binap–Pd–(*S*)-dabn]	5.0	78	80
2	[(*S*)-biphep–Pd–(*S*)-dabn]	5.0	69	78
3	[(*P,S,S*)-tetraphos–Pd–(*S*)-dabn]	2.5	81	86
4	[(*P,S,S*)-tetraphos–Pd–(*S*)-dm-dabn]	2.5	76	85

[a] All reactions were examined through isomerization by enantiopure diamines except for (*S*)-binap. [b] Enantiopurity was determined by chiral GC analysis on a CP-Cyclodextrin-β-2,3,6-M-19 column. [c] Yield of isolated product.

Experimental Section

Dichloroethane (2.0 mL) was added to a mixture of (±)-**1** (22.9 mg, 0.01 mmol) and (*S*)-dabn (6.0 mg, 0.021 mmol) in a 10-mL Schlenk tube under an argon atmosphere, and the reaction mixture was stirred at 80 °C for 2 h. After concentration under reduced pressure, the flask was replenished with argon, and dichloromethane (2.0 mL), ethyl glyoxylate (**8**) (30.6 mg, 0.6 mmol), and methylenecyclohexane (**7**) (48 μL, 0.4 mmol) was added sequentially to the solution. The reaction mixture was stirred at room temperature for 24 h, directly loaded onto a silica-gel column, and eluted with hexane/EtOAc (3:1) to afford (*R*)-**9** in 86% yield as a colorless oil. The enantiomeric excess was determined by chiral GC analysis; GC (column: CP-Cyclodextrin-β-2,3,6-M-19, i.d. 0.25 mm × 25 m, CHROMPACK; carrier gas: nitrogen, 75 kPa; column temperature: 130 °C; injection and detection temperature: 160 °C; split ratio: 100:1), t_R (*R* isomer): 31.3 min, t_R (*S* isomer): 32.4 min; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta =$ 1.26 (t, $J = 6.9$ Hz, 3H), 1.48–1.63 (m, 4H), 1.93–1.99 (m, 4H), 2.24 (dd, $J = 7.8$, 14.1 Hz, 1H), 2.40 (dd, $J = 4.5$, 14.1 Hz, 1H), 2.60 (d, $J =$ 6.3 Hz, 1H), 4.19 (q, $J = 6.9$ Hz, 2H), 5.50 ppm (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 14.4$, 22.4, 23.0, 25.5, 28.7, 43.5, 61.8, 69.6, 126.0, 133.7, 175.9 ppm.

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Keywords: chirality · ene reaction · helical structures · isomerization · palladium

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[5] X-ray crystallographic analysis was performed with a Bruker SMART 1000 diffractometer (graphite monochromator, $Mo_{K\alpha}$ radiation, $\lambda = 0.71073$ Å) at 299 K. Crystal data for $[Pd_2Cl_4(tetraphos)]\cdot 2\,MeOH$ ($C_{66}H_{58}O_2P_4Cl_4Pd_2$): monoclinic, *C*2/*C*, $a =$ 18.796(19) Å, $b = 12.631(13)$ Å, $c = 27.10(3)$ Å, $\alpha = 90°$, $\beta =$ 105.748(18)°, $\gamma = 90°$, $V = 4249.9(3)$ Å^3, $Z = 4$, $\rho_{calcd} =$ 1.486 g cm^{-3}, crystal dimensions $0.37 \times 0.11 \times 0.05$ mm^3, range for data collection $2\theta max = 54.96°$, reflections collected 18277, independent reflections 6783 ($R_{int} = 0.0382$). The structures were solved by direct methods (SHELXL-97); the final cycle of full-matrix least-squares on F^2 was based on 6783 observed reflections ($I > 2\sigma(I)$) and 390 variable parameters, and converged to $R = 0.038$, $Rw = 0.080$, and goodness of fit = 1.001. CCDC-213825 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB21EZ, UK; fax: (+44) 1223-336-033; or deposit@ccdc.cam.ac.uk). ^{1}H NMR (300 MHz, CD_2Cl_2): $\delta = 6.24$–6.28 (m, 3H), 6.77 (dd, $J = 8.1$, 11.7 Hz, 2H), 6.92 (t, $J = 8.1$ Hz, 2H), 7.13–7.18 (m, 2H), 7.23–7.62 (m, 35H), 7.77–7.83 (m, 2H), 7.89 ppm (dd, $J = 7.5$, 12.6 Hz, 4H); ^{31}P NMR (162 MHz, CD_2Cl_2): $\delta = 25.0$ (s, 2P), 27.8 ppm (s, 2P).

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[8] (±)-**1**: ^{31}P NMR (162 MHz, CD_2Cl_2): $\delta = 25.9$ (s, 2P), 29.3 ppm (s, 2P). (*P,S,S*)-**2**: ^{31}P NMR (162 MHz, CD_2Cl_2): $\delta = 22.0$ (d, $J_{P\text{-}P} = 25.9$ Hz, 2P), 25.7 ppm (d, $J_{P\text{-}P} = 25.9$ Hz, 2P).

[9] (*P,S,S*)-**5**: ^{31}P NMR (162 MHz, CD_2Cl_2): $\delta = 24.8$ (d, $J_{P\text{-}P} =$ 19.9 Hz, 2P), 26.3 ppm (d, $J_{P\text{-}P} = 19.9$ Hz, 2P). (*M,R,R*)-**5**: ^{31}P NMR (162 MHz, CD_2Cl_2): $\delta = 22.7$ (d, $J_{P\text{-}P} = 19.1$ Hz, 2P), 28.2 ppm (d, $J_{P\text{-}P} = 19.1$ Hz, 2P).

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