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# How Do Positions of Phosphito Units on a Calix[4]Arene Platform Affect the Enantioselectivity of a Catalytic Reaction?

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1 Article

 2 **How do positions of phosphito units on a calix[4]arene plat-**  
 3 **form affect the enantioselectivity of a catalytic reaction?**

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 8 **Abstract:** Three chiral diphosphites, (*S,S*)-5,17-bis(1,1'-binaphthyl-2,2'-dioxyporphanyloxy)-  
 9 25,26,27,28-tetrapropylcalix[4]arene (**1**), (*S,S*)-5,11,17,23-tetra-*tert*-butyl-25,27-dipropoxy-26,28-  
 10 bis(1,1'-binaphthyl-2,2'-dioxyporphanyloxy)calix[4] arene (**2**) and (*S,S*)-5,11,17,23-tetra-*tert*-butyl-  
 11 25,26-dipropoxy-27,28-bis(1,1'-binaphthyl-2,2'-dioxyporphanyloxy)calix[4]arene (**3**) based on  
 12 conical calix[4]arene were investigated in the rhodium-catalyzed asymmetric hydrogenation of  
 13  $\alpha$ -dehydroamino esters. High conversions were observed after 24 hours under 5 bar of hydrogen  
 14 whatever the employed diphosphite and the chiral induction increases in the order  $1 < 3 < 2$ . This  
 15 may be due to the presence of the calix[4]arene moiety, which by its presence, modifies the second  
 16 coordination sphere of the catalytic center. The larger steric hindrance around the rhodium atom  
 17 leads to the higher enantiomeric excess.

 18 **Keywords:** calix[4]arene; phosphite; rhodium; asymmetric hydrogenation; homogenous catalysis

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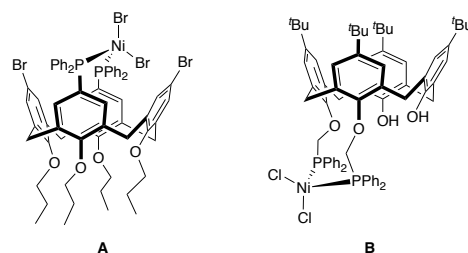
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## 1. Introduction

Since the rational synthetic methods developed by Gutsche 45 years ago via precise cyclocondensation reactions of *para*-substituted phenols with formaldehyde [1-4], calix[4]arene has become a preferred semi-rigid platform for the preparation of convergent ligands [5-9]. Among these, phosphorus-based ligands are often used in transition metal chemistry in particular for catalytic applications [10,11]. The phosphorus atom(s) can be specifically grafted on the upper [12-20] or lower [21-30] rim of the calix[4]arene.

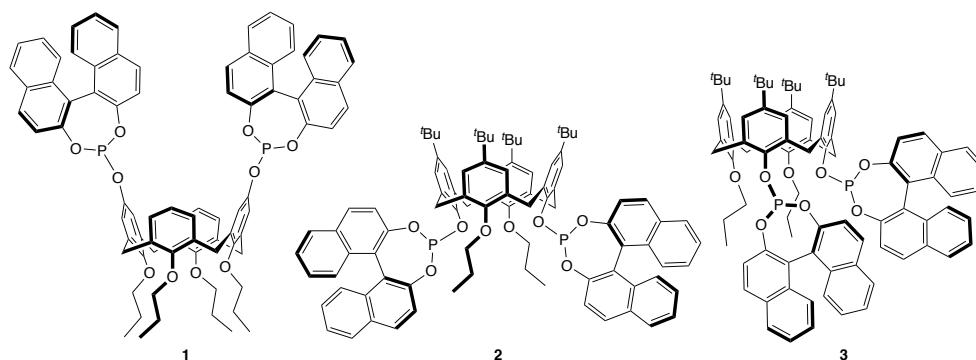
Due to the intrinsic properties of calixarene, its incorporation in the ligand structure presents many advantages such as stabilization of the active species thanks to the steric hindrance generated by the macrocycle [31] or by additional interactions with the auxiliary chains [32,33], increase regioselectivity of the reaction by encapsulation of the catalytic center [34,35], inherent chirality of the calixarene leading to optically active ligands [36-38], intrinsic dynamics of the metal center which allow speeding up elementary steps of catalytic cycles [39,40], supramolecular catalysis by trapping the aromatic substrate in its cavity [41]... However, the study of the structure-activity relationship is rarely studied, especially from the point of view of academic research, the understanding of the mechanistic aspects needs to be improved. In fact, the position of the phosphorus atom(s) on the calixarenyl platform can drastically affect the coordination sphere of the metal and the catalytic outcome as observed, for example, in oligomerization of ethylene [42] with tetrahedral [NiX<sub>2</sub>(diphosphine)] (X = Cl or Br) complexes, namely *cis-P,P'*-dibromo-[5,17-dibromo-11,23-bis(diphenylphosphino)-25,26,27,28-tetrapropyl-oxycalix[4]arene}nickel [43] (**A**) and *cis-P,P'*-dichloro-[5,11,17,23-tetra-*tert*-butyl-25,26-bis(diphenylphosphino-methoxy)-27,28-dihydroxycalix[4]arene} nickel [44] (**B**) using methylaluminumoxane as activator (Figure 1). While pre-catalyst **A** led to the formation of butenes, C<sub>4</sub>-C<sub>12</sub> oligomers with a Schulz-Flory distribution ( $\alpha = 0.22$ ) were

obtained when complex B, which has a significantly higher steric hindrance, was employed.



**Figure 1.** Nickel complexes for oligomerization of ethylene.

The possibility to fine tune the coordination sphere of a catalytic center with the calixarenyl preorganization platform allows the modulation of the steric properties of the ligand to a specific reaction. In this context, we now report the use of calixarenyl diphosphites **1-3** for the asymmetric hydrogenation of  $\alpha$ -dehydroamino esters (Figure 2). The objective of this work is to relate the positioning of the phosphite units on the macrocycle to the efficiency of the chirality transfer from the ligand to the substrates.



**Figure 2.** Calixarenyl diphosphites employed in the present study.

## 2. Materials and Methods

All manipulations were carried out under dry argon. Routine  $^1\text{H}$ ,  $^{13}\text{C}\{^1\text{H}\}$  and  $^{31}\text{P}\{^1\text{H}\}$  spectra were recorded with Bruker FT instruments (AC 300 and 400).  $^1\text{H}$  NMR and  $^{13}\text{C}\{^1\text{H}\}$  spectra were referenced to residual protonated solvents ( $\delta = 7.16$  ppm and 128.08 ppm for  $\text{C}_6\text{D}_6$ , respectively, and 7.26 ppm and 77.16 ppm for  $\text{CDCl}_3$ , respectively).  $^{31}\text{P}$  NMR spectroscopic data are given relative to external  $\text{H}_3\text{PO}_4$ . Chemical shifts and coupling constants are reported in ppm and Hz, respectively. Mass spectra were recorded on a Bruker MicroTOF spectrometer (ESI-TOF). The catalytic solutions were analyzed by using a Varian 3900 gas chromatograph equipped with a CHROMPAK chiral fused silica Chirasil-L-Val column (25 m  $\times$  0.25 mm). (*S,S*)-5,17-Bis(1,1'-binaphthyl-2,2'-dioxypophanyloxy)-25,26,27,28-tetrapropoxy-calix[4]arene (**1**) [45] and (*S,S*)-5,11,17,23-tetra-*tert*-butyl-25,27-dipropoxy-26,28-bis(1,1'-binaphthyl-2,2'-dioxypophanyloxy)calix[4]arene (**2**) [46] were prepared by literature procedures.

### 2.1. Synthesis of 5,11,17,23-tetra-*tert*-butyl-25,26-dipropoxy-27,28-dihydroxycalix[4]arene (**4**) [47]

15,16,17,18-Tetra-*tert*-butyl-25,26,27,28-tetrahydroxycalix[4]arene (2.500 g, 3.8 mmol) dissolved in DMF (500 mL) at 50°C was deprotonated with NaH (60 % dispersion in oil; 0.770 g, 19.3 mmol). After 0.5 h,  $n\text{-PrBr}$  (1.050 g, 0.78 mL, 8.5 mmol) was added and the reaction mixture was heated at 60°C. After 4 days, the solvent was evaporated to dryness and the solid residue was solubilized in  $\text{CH}_2\text{Cl}_2$  (100 mL). The resulting suspension was washed with HCl (2 N, 100 mL). The aqueous layer was extracted with  $\text{CH}_2\text{Cl}_2$

(2 x 50 mL). The combined organic layers were dried over MgSO<sub>4</sub> and concentrated. The desired white solid product was precipitated by addition of methanol, filtered off and dried under vacuum (1.692 g, 60 %). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ = 8.89 (s, 2H, OH), 7.00 (d, 2H, CH arom, <sup>4</sup>J = 2.4 Hz), 6.98 (d, 2H, CH arom, <sup>4</sup>J = 2.8 Hz), 6.97 (d, 2H, CH arom, <sup>4</sup>J = 2.8 Hz), 6.91 (d, 2H, CH arom, <sup>4</sup>J = 2.4 Hz), 4.49 and 3.32 (AB system, 2H, ArCH<sub>2</sub>Ar, <sup>2</sup>J = 12.6 Hz), 4.32 and 3.34 (AB system, 4H, ArCH<sub>2</sub>Ar, <sup>2</sup>J = 12.9 Hz), 4.29 and 3.32 (AB system, 2H, ArCH<sub>2</sub>Ar, <sup>2</sup>J = 13.2 Hz), 4.08-4.00 (m, 4H, OCH<sub>2</sub>), 3.90-3.82 (m, 4H, OCH<sub>2</sub>), 2.08 (hex, 4H, CH<sub>2</sub>CH<sub>3</sub>, <sup>3</sup>J = 7.5 Hz), 1.26 (s, 18H, C(CH<sub>3</sub>)<sub>3</sub>), 1.12 (t, 6H, CH<sub>2</sub>CH<sub>3</sub>, <sup>3</sup>J = 7.5 Hz), 1.10 (s, 18H, C(CH<sub>3</sub>)<sub>3</sub>) ppm.

### 2.2. Synthesis of (S,S)-5,11,17,23-tetra-tert-butyl-25,26-dipropoxy-27,28-bis(1,1'-binaphthyl-2,2'-dioxiphosphanyloxy)calix[4]arene (3)

5,11,17,23-Tetra-tert-butyl-25,26-dipropoxy-27,28-dihydroxycalix[4]arene (4) (0.600 g, 0.82 mmol) in refluxing toluene (30 mL) was deprotonated with NaH (60% dispersion in oil, 0.072 g, 1.80 mmol). After 24 h, a solution of [(S)-(1,1'-binaphthalene-2,2'-diyl)]chlorophosphite (0.718 g, 2.05 mmol) in toluene (15 mL) was added at 0°C. The resulting reaction mixture was stirred at room temperature for additional 2 h. The crude solution was filtered through Al<sub>2</sub>O<sub>3</sub>, which was washed twice with toluene (2 x 15 mL). The desired white solid product 3 was obtained by evaporation of the toluene under reduce pressure (0.792 g, yield 71 %). <sup>1</sup>H NMR (300 MHz, C<sub>6</sub>D<sub>6</sub>): δ = 8.10 (d, 1H, CH arom, <sup>3</sup>J = 8.7 Hz), 7.78 (d, 1H, CH arom, <sup>3</sup>J = 8.7 Hz), 7.71 (d, 1H, CH arom, <sup>3</sup>J = 8.1 Hz), 7.63 (d, 1H, CH arom, <sup>3</sup>J = 8.1 Hz), 7.60-7.53 (m, 3H, CH arom), 7.47 (d, 1H, CH arom, <sup>3</sup>J = 8.7 Hz), 7.29-7.22 (m, 4H, CH arom), 7.13-7.02 (m, 12H, CH arom), 7.00-6.93 (m, 3H, CH arom), 6.92-6.90 (m, 2H, CH arom), 6.76 (brs, 2H, CH arom), 6.03 (brs, 1H, CH arom), 5.32 and 3.48 (AB system, 2H, ArCH<sub>2</sub>Ar, <sup>2</sup>J = 13.2 Hz), 4.97 and 3.46 (AB system, 2H, ArCH<sub>2</sub>Ar, <sup>2</sup>J = 12.9 Hz), 4.34 and 3.14 (AB system, 2H, ArCH<sub>2</sub>Ar, <sup>2</sup>J = 12.3 Hz), 4.32 and 3.38 (AB system, 2H, ArCH<sub>2</sub>Ar, <sup>2</sup>J = 13.5 Hz), 3.78-3.52 (m, 4H, OCH<sub>2</sub>), 1.81-1.66 (m, 4H, CH<sub>2</sub>CH<sub>3</sub>), 1.45 (s, 9H, C(CH<sub>3</sub>)<sub>3</sub>), 1.39 (s, 9H, C(CH<sub>3</sub>)<sub>3</sub>), 1.09 (s, 9H, C(CH<sub>3</sub>)<sub>3</sub>), 0.99 (s, 9H, C(CH<sub>3</sub>)<sub>3</sub>), 0.95 (t, 3H, CH<sub>2</sub>CH<sub>3</sub>, <sup>3</sup>J = 7.4 Hz), -0.17 (t, 3H, CH<sub>2</sub>CH<sub>3</sub>, <sup>3</sup>J = 7.5 Hz); <sup>13</sup>C{<sup>1</sup>H} NMR (75 MHz, C<sub>6</sub>D<sub>6</sub>): δ = 154.30-122.35 (arom C's), 78.38 (s, OCH<sub>2</sub>), 76.28 (s, OCH<sub>2</sub>), 34.31 (s, C(CH<sub>3</sub>)<sub>3</sub>), 34.15 (s, C(CH<sub>3</sub>)<sub>3</sub>), 34.01 (s, C(CH<sub>3</sub>)<sub>3</sub>), 32.81 (s, ArCH<sub>2</sub>Ar), 32.61 (s, ArCH<sub>2</sub>Ar), 32.36 (s, ArCH<sub>2</sub>Ar), 32.11 (s, C(CH<sub>3</sub>)<sub>3</sub>), 31.96 (s, C(CH<sub>3</sub>)<sub>3</sub>), 31.55 (s, ArCH<sub>2</sub>Ar), 31.40 (s, C(CH<sub>3</sub>)<sub>3</sub>), 23.62 (s, CH<sub>2</sub>CH<sub>3</sub>), 22.90 (s, CH<sub>2</sub>CH<sub>3</sub>), 10.92 (s, CH<sub>2</sub>CH<sub>3</sub>), 8.84 (s, CH<sub>2</sub>CH<sub>3</sub>); <sup>31</sup>P{<sup>1</sup>H} NMR (121 MHz, C<sub>6</sub>D<sub>6</sub>): δ = 150.7 (s, OP(OAr)<sub>2</sub>) ppm. Elemental analysis (%): calcd for C<sub>90</sub>H<sub>90</sub>P<sub>2</sub>O<sub>8</sub> (1361.62): C 79.39, H 6.66; found: C 79.16, H 6.84.

### 2.3. Synthesis of cis-P,P'-[(S,S)-5,11,17,23-tetra-tert-butyl-25,27-dipropoxy-26,28-bis(1,1'-binaphthyl-phosphite)calix[4]arene]-1,5-cyclooctadiene]rhodium(I) tetrafluoroborate (5)

Ligand 2 (0.284 g, 0.21 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (5 mL) was added drop to drop to a solution of [Rh(cod)<sub>2</sub>]BF<sub>4</sub> (0.077 g, 0.19 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (250 mL). After 16 h, the resulted solution was concentrated to ca. 3 mL and the complex 5 was precipitated out after addition of hexane (50 mL). The orange precipitate was filtered off and dried under vacuum (0.280 g, 89 % yield). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ = 8.24 (d, 2H, CH arom, <sup>3</sup>J = 8.8 Hz), 8.03 (d, 2H, CH arom, <sup>3</sup>J = 8.8 Hz), 7.99 (d, 2H, CH arom, <sup>3</sup>J = 8.1 Hz), 7.78 (d, 2H, CH arom, <sup>3</sup>J = 8.1 Hz), 7.68 (d, 2H, CH arom, <sup>3</sup>J = 8.9 Hz), 7.51-7.35 (m, 6H, CH arom), 7.24-7.10 (m, 4H, CH arom), 6.98 (d, 2H, CH arom, <sup>3</sup>J = 8.6 Hz), 6.86 (d, 2H, CH arom, <sup>3</sup>J = 8.6 Hz), 6.79 (d, 2H, CH arom, <sup>4</sup>J = 2.1 Hz), 6.58 (d, 2H, CH arom, <sup>4</sup>J = 2.4 Hz), 6.28 (d, 2H, CH arom, <sup>4</sup>J = 2.1 Hz), 6.23 (d, 2H, CH arom, <sup>4</sup>J = 2.1 Hz), 6.19-6.09 (m, 2H, CH of cod), 5.01 and 2.98 (AB system, 4H, ArCH<sub>2</sub>Ar, <sup>2</sup>J = 13.5 Hz), 4.89 and 3.31 (AB system, 4H, ArCH<sub>2</sub>Ar, <sup>2</sup>J = 12.7 Hz), 4.46-4.38 (m, 2H, OCH<sub>2</sub>), 4.36-4.23 (m, 2H, CH of cod), 4.11-3.97 (m, 2H, OCH<sub>2</sub>), 2.74-2.58 (m, 2H, CH<sub>2</sub> of cod), 2.40-2.33 (m, 2H, CH<sub>2</sub> of cod), 2.33-2.10 (m, 4H, CH<sub>2</sub>CH<sub>3</sub>), 1.65-1.53 (m, 2H, CH<sub>2</sub> of cod), 1.16 (t, 6H, CH<sub>2</sub>CH<sub>3</sub>, <sup>3</sup>J = 7.4 Hz), 1.09-1.04 (m, 2H, CH<sub>2</sub> of cod), 1.01 (s, 18H, C(CH<sub>3</sub>)<sub>3</sub>), 0.74 (s, 18H, C(CH<sub>3</sub>)<sub>3</sub>); <sup>13</sup>C{<sup>1</sup>H} NMR (75 MHz,

CDCl<sub>3</sub>):  $\delta$  = 151.16-119.71 (arom C's), 106.66 (s, CH of cod), 95.99 (s, CH of cod), 77.92 (s, OCH<sub>2</sub>), 34.97 (s, CH<sub>2</sub> of cod), 33.69 (s, C(CH<sub>3</sub>)<sub>3</sub>), 33.61 (s, CH<sub>2</sub> of cod), 33.60 (s, ArCH<sub>2</sub>Ar), 33.61 (s, CH<sub>2</sub> of cod), 33.58 (s, C(CH<sub>3</sub>)<sub>3</sub>), 33.36 (s, ArCH<sub>2</sub>Ar), 31.10 (s, C(CH<sub>3</sub>)<sub>3</sub>), 30.90 (s, C(CH<sub>3</sub>)<sub>3</sub>), 26.79 (s, CH<sub>2</sub> of cod), 23.54 (s, CH<sub>2</sub>CH<sub>3</sub>), 10.27 (s, CH<sub>2</sub>CH<sub>3</sub>); <sup>31</sup>P{<sup>1</sup>H} NMR (121 MHz, CDCl<sub>3</sub>):  $\delta$  = 120.7 (d, OP(OAr)<sub>2</sub>, <sup>1</sup>J<sub>P-Rh</sub> = 256.8 Hz) ppm. MS (ESI TOF), m/z: 1571.61 [M - BF<sub>4</sub>]<sup>+</sup> and 1463.54 [M - C<sub>8</sub>H<sub>12</sub> - BF<sub>4</sub>]<sup>+</sup> expected isotopic profiles. Elemental analysis (%): calcd for C<sub>98</sub>H<sub>102</sub>BF<sub>4</sub>O<sub>8</sub>P<sub>2</sub>Rh (1659.51): C 70.93, H 6.19; found: C 70.86, H 5.94.

#### 2.4. General procedure for the hydrogenation experiments

Hydrogenation experiments were carried out in a glass-lined, 100 mL stainless steel autoclave containing a magnetic stirring bar. The reactor was flushed with nitrogen and charged with [Rh(cod)<sub>2</sub>]BF<sub>4</sub> (0.01 mmol), ligand (0.01 mmol) and CH<sub>2</sub>Cl<sub>2</sub> (10 mL). The resulting mixture was stirred at room temperature for 0.5 h. The  $\alpha$ -dehydroamino esters (1.00 mmol) was then added. The autoclave was flushed twice with H<sub>2</sub>, pressurized to 5 bars and stirred at room temperature for 24 h. After depressurization of the reactor, the solution was passed through a short silica column to remove the catalyst. The conversion and the enantioselectivity were determined by <sup>1</sup>H NMR spectroscopy and by chiral GC analysis using a CHROMPAK chiral fused silica Chirasil-L-Val column (25 m  $\times$  0.25 mm), respectively.

*N*-Acetyl-phenylalanine methyl ester (**7a**) <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz):  $\delta$  = 7.31-7.21 (m, 3H, CH arom.), 7.09 (dd, 2H, CH arom., <sup>3</sup>J = 7.7 Hz, <sup>4</sup>J = 1.9 Hz), 6.05 (d, 1H, NH, <sup>3</sup>J = 7.8 Hz), 4.87 (dt, 1H, CH<sub>2</sub>CHNH, <sup>3</sup>J = 7.8 Hz, <sup>3</sup>J = 5.8 Hz), 3.71 (s, 3H, CO<sub>2</sub>CH<sub>3</sub>), 3.12 and 3.09 (ABX system, 2H, CH<sub>2</sub>CH, <sup>2</sup>J = 13.8 Hz, <sup>3</sup>J = 5.8 Hz), 1.97 (s, 3H, NHCOCH<sub>3</sub>) ppm.

*N*-Acetyl-4-fluoro-phenylalanine methyl ester (**7b**) <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz):  $\delta$  = 7.07-6.93 (m, 4H, CH arom.), 6.02 (d, 1H, NH, <sup>3</sup>J = 7.6 Hz), 4.85 (dt, 1H, CH<sub>2</sub>CHNH, <sup>3</sup>J = 7.6 Hz, <sup>3</sup>J = 5.7 Hz), 3.71 (s, 3H, CO<sub>2</sub>CH<sub>3</sub>), 3.12 and 3.04 (ABX system, 2H, CH<sub>2</sub>CH, <sup>2</sup>J = 14.1 Hz, <sup>3</sup>J = 5.7 Hz), 1.98 (s, 3H, NHCOCH<sub>3</sub>) ppm.

*N*-Acetyl-4-chloro-phenylalanine methyl ester (**7c**) <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz):  $\delta$  = 7.23 (d, 2H, CH arom., <sup>3</sup>J = 8.3 Hz), 7.01 (d, 2H, CH arom., <sup>3</sup>J = 8.3 Hz), 6.18 (brs, 1H, NH), 4.83 (dt, 1H, CH<sub>2</sub>CHNH, <sup>3</sup>J = 7.8 Hz, <sup>3</sup>J = 5.8 Hz), 3.69 (s, 3H, CO<sub>2</sub>CH<sub>3</sub>), 3.98 and 3.01 (ABX system, 2H, CH<sub>2</sub>CH, <sup>2</sup>J = 13.8 Hz, <sup>3</sup>J = 5.8 Hz), 1.95 (s, 3H, NHCOCH<sub>3</sub>) ppm.

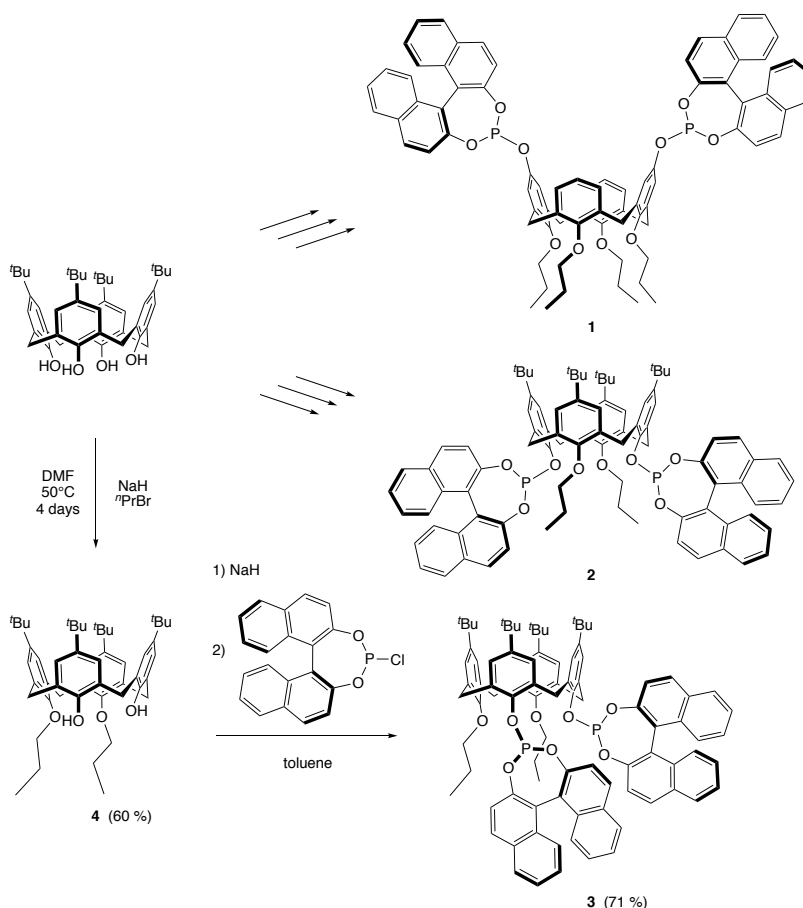
*N*-Acetyl-3,4-dichloro-phenylalanine methyl ester (**7d**) <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz):  $\delta$  = 7.33 (d, 1H, CH arom., <sup>3</sup>J = 8.3 Hz), 7.18 (d, 1H, CH arom., <sup>4</sup>J = 2.2 Hz), 6.93 (dd, 1H, CH arom., <sup>3</sup>J = 8.3 Hz, <sup>4</sup>J = 2.2 Hz), 6.19 (d, 1H, NH, <sup>3</sup>J = 7.6 Hz), 4.85 (dt, 1H, CH<sub>2</sub>CHNH, <sup>3</sup>J = 7.6 Hz, <sup>3</sup>J = 5.9 Hz), 3.72 (s, 3H, CO<sub>2</sub>CH<sub>3</sub>), 3.11 and 2.99 (ABX system, 2H, CH<sub>2</sub>CH, <sup>2</sup>J = 13.9 Hz, <sup>3</sup>J = 5.9 Hz), 1.98 (s, 3H, NHCOCH<sub>3</sub>) ppm.

### 3. Results

Starting from the 5,11,17,23-tetra-*tert*-butyl-25,26,27,28-tetrol-calix[4]arene, two diphosphites in which the phosphito units are grafted on distal aromatic either on the upper or on the lower rim of the macrocycle, namely (*S,S*)-5,17-bis(1,1'-binaphthyl-2,2'-dioxyphosphan-yloxy)-25,26,27,28-tetrapropoxy-calix[4]arene (**1**) [45] and (*S,S*)-5,11,17,23-tetra-*tert*-butyl-25,27-dipropoxy-26,28-bis(1,1'-binaphthyl-2,2'-dioxyphosphan-yloxy)calix[4] arene (**2**) [46] were prepared following previous reports of our group. The third diphosphite was obtained in two steps, firstly a double alkylation of two proximally phenolic units with NaH and <sup>n</sup>PrBr in DMF, which led after 4 days at room temperature to the O-dialkylated precursor **4** [47] in 60 % yield. In keeping with a Cs-symmetrical structure, its <sup>1</sup>H NMR spectrum displays three distinct AB patterns for the diastereotopic ArCH<sub>2</sub>Ar protons at 4.49/3.32 (<sup>2</sup>J = 12.6 Hz), 4.32/3.34 (<sup>2</sup>J = 12.9 Hz), and 4.29/3.32 (<sup>2</sup>J = 13.2 Hz) ppm integrated for 2, 4 and 2 protons, respectively.

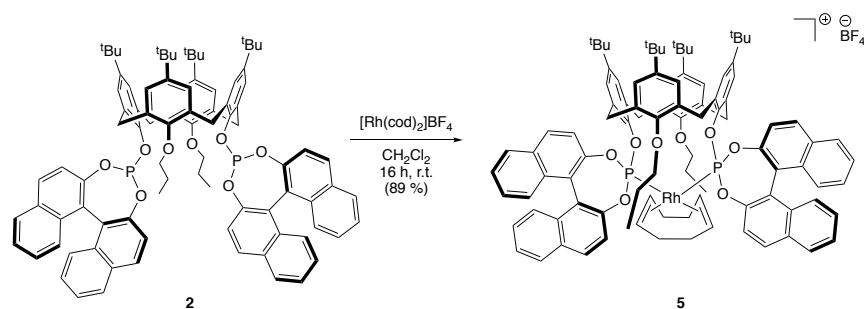
The second step consists of a double deprotonation of intermediate with NaH **4** followed by a reaction with (*S*)-(1,1'-binaphthalene-2,2'-diyl)chlorophosphite, which led to the diphosphite **3** (Scheme 1). After workup, diphosphite **3** was isolated in 71 % yield

and was characterized by a singlet peak at 150.7 ppm in its  $^{31}\text{P}$  NMR spectrum. As anticipated, the “cone” conformation of the calix[4]arene was inferred from the corresponding  $^{13}\text{C}$  NMR spectrum, which shows four signals in the range 32.81–31.55 ppm for the  $\text{ArCH}_2\text{Ar}$  groups [48]. Consistent with a  $C_1$ -symmetrical compound, the  $^1\text{H}$  NMR spectrum displays four distinct AB patterns for the  $\text{ArCH}_2\text{Ar}$  protons at 5.32/3.48 ( $^2J = 13.2$  Hz), 4.97/3.46 ( $^2J = 12.9$  Hz), 4.34/3.14 ( $^2J = 12.3$  Hz) and 4.32/3.38 ( $^2J = 13.5$  Hz) ppm.



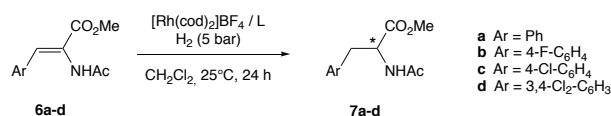
**Scheme 1.** Synthesis of diphosphites 1-3.

The reaction of the lower rim distally substituted diphosphito-calixarene **2** with  $[\text{Rh}(\text{cod})_2]\text{BF}_4$  ( $\text{cod} = 1,5$ -cyclooctadiene) in  $\text{CH}_2\text{Cl}_2$  (0.7 mM) gave, after work-up, the complex **5** in 89 % yield as an orange solid (Scheme 2). Owing to the large separation between the two coordinated atoms, 12 bonds, exclusive formation of a  $P,P$ -chelate rhodium complex was occurred. The structure of the complex was deduced from its mass spectrum, which shows strong peaks corresponding to the  $[\text{M} - \text{BF}_4]^+$  and  $[\text{M} - \text{C}_8\text{H}_{12} - \text{BF}_4]^+$  cations at  $m/z = 1571.61$  and  $1463.54$ , respectively. NMR spectra are consistent with a  $C_2$ -symmetrical molecule: a doublet centered at 120.7 ppm ( $^1J_{\text{P-Rh}} = 256.8$  Hz) and two AB systems for the diastereotopic  $\text{ArCH}_2\text{Ar}$  protons at 5.01/2.98 ( $^2J = 13.5$  Hz) and 4.89/3.31 ( $^2J = 12.7$  Hz) ppm are observed in the corresponding  $^{31}\text{P}$  and  $^1\text{H}$  NMR spectra, respectively. Note that when the synthesis of complex **5** was performed in lower-dilution conditions (10 mM), formation of by-products was observed (85 % purity). Nevertheless, with this mixture of complexes, Sandoval *and coll.* observed important enantiomeric excesses in the asymmetric hydrogenation of methyl-(*Z*)-2-(acetamido)acrylate and methyl-(*Z*)-2-(acetamido)cinnamate [49].



Scheme 2. Formation of  $[\text{Rh}(\mathbf{2})(\text{cod})]\text{BF}_4$  complex (**5**).

Four different  $\alpha$ -dehydroamino esters, namely (*Z*)-*N*-acetyl-dehydro-phenylalanine methyl ester (**6a**), (*Z*)-*N*-acetyl-dehydro-4-fluoro-phenylalanine methyl ester (**6b**), (*Z*)-*N*-acetyl-dehydro-4-chloro-phenylalanine methyl ester (**6c**) and (*Z*)-*N*-acetyl-dehydro-3,4-dichloro-phenylalanine methyl ester (**6d**) were used to assess the performance of diphosphites **1-3** in the rhodium catalyzed asymmetric hydrogenation (Scheme 3).



Scheme 3. Enantiomeric hydrogenation of  $\alpha$ -dehydroamino esters **6a-d**.

In the following tests, the catalytic system was *in situ* generated by mixing an equimolar amount (0.01 mmol, 1 mol %) of  $[\text{Rh}(\text{cod})_2]\text{BF}_4$  as metal precursor and ligand (**1-3**) in  $\text{CH}_2\text{Cl}_2$ . The resulting solution was stirred at room temperature for 30 minutes before the addition of the  $\alpha$ -dehydroamino ester (**6a-d**; 1 mmol). The reaction mixture was stirred under 5 bar of hydrogen for an additional 24 h.  $^1\text{H}$  NMR carried out on the reaction mixtures revealed that using ligands **1-3**, the conversion was increased in the order  $1 < 2 < 3$  (Table 1). As example, under the latter catalytic conditions, (*Z*)-*N*-acetyl-dehydro-4-fluoro-phenylalanine methyl ester (**6b**) was reduced into *N*-acetyl-4-fluoro-phenylalanine methyl ester (**7b**) in 83, 92 and 100 % conversion when diphosphites **1**, **2** and **3** were employed, respectively (Table 1, entries 2, 6 and 11).

The reduced products **7a-d** were obtained with modest enantiomeric excesses (*ee*) 48-57 % when diphosphite **1** was employed (Table 1, entries 1-4). Slightly higher *ee* values, 58-66 %, were measured when ligand **3** was used (Table 1, entries 10-13). The more important *ee* values, higher than 90 %, were measured when the calixarenyl diphosphite **2** was associated with the rhodium precursor (Table 1, entries 5-8). Using the latter catalytic system, *N*-acetyl-4-chloro-phenylalanine methyl ester (**7c**) and *N*-acetyl-4-fluoro-phenylalanine methyl ester (**7b**) were obtained with *ee* values of 94 and 95 %, respectively. Note that, under the previous catalytic conditions, repeating the hydrogenation of  $\alpha$ -dehydroamino ester **6a** with the well defined  $[\text{Rh}(\mathbf{2})(\text{cod})]\text{BF}_4$  (**5**) did not change the catalytic outlook, the reduced product **7a** was quantitatively formed (*ee* = 92 %) (Table 1, entry 9). No reduction was occurred when the dimeric  $[\text{RhCl}(\text{cod})]_2$  complex was employed as rhodium source.

It is interesting to note that only few examples of asymmetric hydrogenation of  $\alpha$ -dehydroamino esters using diphosphites derived from optically pure binol were reported. The nature of the bridge linking the two phosphorus atoms has a direct effect on the catalytic outcome. In fact, when D-glucose [50] or *N*-phenyldiethanolamine [51] were incorporated in the ligand, low *ee* values, 28-32 %, were measured in the hydrogenation of (*Z*)-*N*-acetyl-dehydro-phenylalanine methyl ester (**6a**). In contrast, important enantiomeric excesses, similar to those obtained with our calixarenyl ligand **2**, were obtained by Fan *and coll.* using diphosphite-containing metallacrown ether as ligand [52] and by Xia *and coll.* with a norbornane backbone [53].

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**Table 1.** Enantiomeric hydrogenation of  $\alpha$ -dehydroamino esters **6a-d**.<sup>1</sup>

Entry	Substrate (Ar)	Ligand	Conversion (%) <sup>2</sup>	<i>ee</i> (%) <sup>3</sup>
1	<b>6a</b> (Ar = Ph)	<b>1</b>	100	57 (R)
2	<b>6b</b> (Ar = 4-F-C <sub>6</sub> H <sub>4</sub> )	<b>1</b>	83	48 (R)
3	<b>6c</b> (Ar = 4-Cl-C <sub>6</sub> H <sub>4</sub> )	<b>1</b>	86	57 (R)
4	<b>6d</b> (Ar = 3,4-Cl <sub>2</sub> -C <sub>6</sub> H <sub>3</sub> )	<b>1</b>	91	52 (R)
5	<b>6a</b> (Ar = Ph)	<b>2</b>	100	91 (R)
6	<b>6b</b> (Ar = 4-F-C <sub>6</sub> H <sub>4</sub> )	<b>2</b>	92	95 (R)
7	<b>6c</b> (Ar = 4-Cl-C <sub>6</sub> H <sub>4</sub> )	<b>2</b>	97	94 (R)
8	<b>6d</b> (Ar = 3,4-Cl <sub>2</sub> -C <sub>6</sub> H <sub>3</sub> )	<b>2</b>	100	90 (R)
9 <sup>4</sup>	<b>6a</b> (Ar = Ph)	<b>2</b>	100	92 (R)
10	<b>6a</b> (Ar = Ph)	<b>3</b>	100	62 (R)
11	<b>6b</b> (Ar = 4-F-C <sub>6</sub> H <sub>4</sub> )	<b>3</b>	100	66 (R)
12	<b>6c</b> (Ar = 4-Cl-C <sub>6</sub> H <sub>4</sub> )	<b>3</b>	100	58 (R)
13	<b>6d</b> (Ar = 3,4-Cl <sub>2</sub> -C <sub>6</sub> H <sub>3</sub> )	<b>3</b>	100	63 (R)

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<sup>1</sup> Reagents and conditions: [Rh(cod)<sub>2</sub>]BF<sub>4</sub> (1 mol %), ligand (1 mol %), CH<sub>2</sub>Cl<sub>2</sub> (12 mL), P(H<sub>2</sub>) = 5 bar, 25°C, 24 h;

<sup>2</sup> conversions were determined by <sup>1</sup>H NMR spectroscopy;

<sup>3</sup> enantiomeric excess were determined by chiral GC analysis (CHROMPAK, 25 m × 0.25 mm, Chirasil-L-Val);

<sup>4</sup> with [Rh(2)(cod)]BF<sub>4</sub> (1 mol %).

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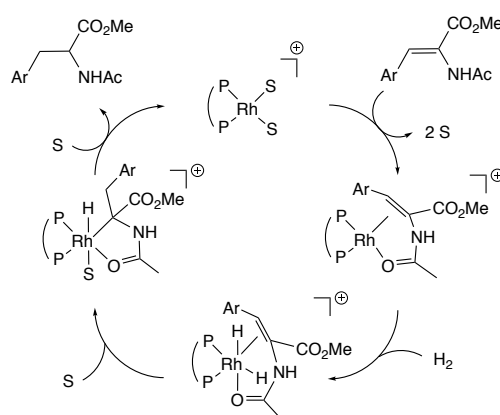
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#### 4. Discussion

As interfered from Table 1, the nature of the diphosphite has a direct influence on the results of the asymmetric hydrogenation of the  $\alpha$ -dehydroamino esters **6a-d**, the chiral induction increases in the order **1** < **3** < **2**. Based on the mechanism described by Halpern *and coll.* (Scheme 4) [54-56], these differences would not come from electronic factors (in each case P(OAr)<sub>3</sub> moieties), but from steric factors generated by the bridge between the two phosphorus atoms, i.e. by the calix[4]arene platform.

**Scheme 4.** Halpern's mechanism of hydrogenation.

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## 5. Conclusions

In summary, we have described the synthesis of optically pure diphosphite in which the two phosphorus atoms are grafted on two proximally phenolic rings of a calix[4]arene. The latter compound and two related calixarenyl diphosphites have been employed in the asymmetric hydrogenation of  $\alpha$ -dehydroamino esters. With these three ligands, high conversions were observed after 24 hours under 5 bar of hydrogen. We have shown that the position of the two phosphito units on the calixarene platform has a determining role in the chirality transfer from the ligand to the substrate and can be directly related to the steric hindrance generated by the second coordination sphere [58] of the ligand, in other words by the calixarenyl skeleton. In fact, the highest enantiomeric excess, 95 %, was obtained with diphosphite **2**, which was able to encapsulate the catalytic center inside a molecular pocket generated by the naphthyl substituents and the auxiliary side groups. Further studies aim at exploiting the structural diversity offered by the calix[4]arene platform in homogeneous catalysis.

**Supplementary Materials:** The following supporting information can be downloaded at: [www.mdpi.com/xxx/s1](http://www.mdpi.com/xxx/s1),  $^1\text{H}$ ,  $^{13}\text{C}$  and  $^{31}\text{P}$  NMR spectra of compounds **3-5** and **7a-d** are given.

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## References

1. Gutsche, C. D.; Muthukrishnan, R. Calixarenes. 1. Analysis of the product mixtures produced by the base-catalyzed condensation of formaldehyde with para-substituted phenols. *J. Org. Chem.* **1978**, *43*, 4905-4906.
2. Gutsche, C. D.; Dhawan, B.; No, K. H.; Muthukrishnan, R. Calixarenes. 4. The synthesis, characterization, and properties of the calixarenes from p-tert-butylphenol. *J. Am. Chem. Soc.* **1981**, *103*, 3782-3792.
3. Gutsche, C. D. Calixarenes. *Acc. Chem. Res.* **1983**, *16*, 161-170.
4. Gutsche, C. D.; Iqbal, M.; Stewart, D. Calixarenes. 18. Synthesis procedures for p-tert -butylcalix[4]arene. *J. Org. Chem.* **1986**, *51*, 742-745.
5. Wieser, C.; Dieleman, C. B.; Matt, D. Calixarene and resorcinarene ligands in transition metal chemistry. *Coord. Chem. Rev.* **1997**, *165*, 93-161.
6. Sliwa, W. Calixarene complexes with transition metal, lanthanide and actinide ions. *Croat. Chem. Acta* **2002**, *75*, 131-153.
7. Sliwa, W. Calixarene complexes with transition metal ions. *J. Incl. Phenom. Macrocycl. Chem.* **2005**, *52*, 13-37.
8. Homden, D. M.; Redshaw, C. The use of calixarenes in metal-based catalysis. *Chem. Rev.* **2008**, *108*, 5086-5130.
9. Santoro, O.; Redshaw, C. Metalcalix[n]arenes in catalysis: A 13-year update. *Coord. Chem. Rev.* **2021**, *448*, 214173.
10. Sémeril, D.; Matt, D. Synthesis and catalytic relevance of P(III) and P(V)-functionalised calixarenes and resorcinarenes. *Coord. Chem. Rev.* **2014**, *279*, 58-95.
11. Bauder, C.; Sémeril, D. Styrene hydroformylation with cavity-shaped ligands. *Eur. J. Inorg. Chem.* **2019**, 4951-4965.
12. Hamada, F.; Fukugaki, T.; Murai, K.; Orr, G. W.; Atwood, J. L. Liquid-liquid extraction of transition and alkali cations by a new calixarene: diphenylphosphino calix[4]arene methyl ether. *J. Inclusion Phenom.* **1991**, *10*, 57-61.
13. Shimizu, S.; Shirakawa, S.; Sasaki, Y.; Hirai, C. Novel Water-soluble calix[4]arene ligands with phosphane-containing groups for dual functional metal-complex catalysts: the biphasic hydroformylation of water-insoluble olefins. *Angew. Chem. Int. Ed.* **2000**, *39*, 1256-1259.
14. Fang, X.; Scott, B. L.; Watkin, J. G.; Carter, C. A. G.; Kubas, G. J. Metal complexes based on an upper-rim calix[4]arene phosphine ligand. *Inorg. Chim. Acta* **2001**, *317*, 276-281.

- 367 15. Mongrain, P.; Harvey, P. D. An original calix[4]arene-containing oligomer/polymer catalyst for homogeneous  
368 hydroformylation. *Macromol. Rapid Commun.* **2008**, *29*, 1752-1757.
- 369 16. Khiri, N.; Bertrand, E.; Ondel-Eymin, M.-J.; Rousselin, R.; Bayardon, J.; Harvey, P. D.; Jugé, S. Enantioselective hydrogenation  
370 catalysis aided by a  $\sigma$ -bonded calix[4]arene to a P-chirogenic aminophosphane phosphinite rhodium complex. *Organometallics*  
371 **2010**, *29*, 3622-3631.
- 372 17. Monnereau, L.; Sémeril, D.; Matt, D. High efficiency of cavity-based triaryl-phosphines in nickel-catalysed  
373 Kumada-Tamao-Corriu cross-coupling. *Chem. Commun.* **2011**, *47*, 6626-6628.
- 374 18. Khiri-Meribout, N.; Bertrand, E.; Bayardon, J.; Eymin, M.-J.; Rousselin, Y.; Cattey, H.; Fortin, D.; Harvey, P. D.; Jugé, S.  
375 P-Chirogenic phosphines supported by calix[4]arene: New insight into palladium-catalyzed asymmetric allylic substitution.  
376 *Organometallics* **2013**, *32*, 2827-2839.
- 377 19. Elaieb, F.; Hedhli, A.; Sémeril, D.; Matt, D. Arylcalixarenyl phosphines in palladium-catalyzed Suzuki-Miyaura cross-coupling  
378 reactions. *Eur. J. Org. Chem.* **2016**, 1867-1873.
- 379 20. Elaieb, F.; Sémeril, D.; Matt, D.; Pfeffer, M.; Bouit, P.-A.; Hissler, M.; Gourlaouen, C.; Harrowfield, J. Calix[4]arene-fused  
380 phospholes. *Dalton Trans.* **2017**, *46*, 9833-9845.
- 381 21. Csók, Z.; Szalontai, G.; Czira, G.; Kollár, L. Carbonylation (hydroformylation and hydrocarbalkoxylation) reactions in the  
382 presence of transition metal: *p*-tert-butyl-calix[4]arene-based phosphine and phosphinite systems. *J. Organomet. Chem.* **1998**,  
383 *570*, 23-29.
- 384 22. Paciello, R.; Siggel, L.; Röper, M. Chelated bisphosphites with a calix[4]arene backbone: New ligands for rhodium-catalyzed  
385 low-pressure hydroformylation with controlled regioselectivity. *Angew. Chem. Int. Ed.* **1999**, *38*, 1920-1923.
- 386 23. Jeunesse, C.; Dieleman, C.; Steyer, S.; Matt, D. Calix[4]arene-derived diphosphines, diphosphinites and diphosphites as  
387 chelating ligands for transition metal ions. Encapsulation of silver(I) in a calix-crown diphosphite. *J. Chem. Soc., Dalton Trans.*  
388 **2001**, 881-892.
- 389 24. Kunze, C.; Selent, D.; Neda, I.; Freytag, M.; Jones, P. G.; Schmutzler, R.; Baumann, W.; Börner, A. Calix[4]arene-based  
390 bis-phosphonites, bis-phosphites, and bis-O-acyl-phosphites as ligands in the rhodium(I)-catalyzed hydroformylation of  
391 1-octene. *Z. Anorg. Allg. Chem.* **2002**, *628*, 779-787.
- 392 25. Marson, A.; Freixa, Z.; Kamer, P. C. J.; van Leeuwen, P. W. N. M. Chiral calix[4]arene-based diphosphites as ligands in the  
393 asymmetric hydrogenation of prochiral olefins. *Eur. J. Inorg. Chem.* **2007**, 4587-4591.
- 394 26. Sémeril, D.; Matt, D.; Toupet, L. Highly regioselective hydroformylation with hemispherical chelators. *Chem. Eur. J.* **2008**, *14*,  
395 7144-7155.
- 396 27. Maji, P.; Mahalakshmi, L.; Krishnamurthy, S. S.; Nethaji, M. Cyclometalated complexes derived from calix[4]arene  
397 bisphosphites and their catalytic applications in cross-coupling reactions. *J. Organomet. Chem.* **2011**, *696*, 3169-3179.
- 398 28. Cobley, C. J.; Pringle, P. G. A water-soluble phosphite derived from sulfonated calix[4]arene. The remarkable stability of its  
399 rhodium complexes and two phase hydroformylation studies. *Catal. Sci. Technol.* **2011**, *1*, 239-242.
- 400 29. Hirasawa, K.; Tanaka, S.; Horiuchi, T.; Kobayashi, T.; Sato, T.; Morohashi, N.; Hattori, T. Pd(II) Complexes ligated by  
401 1,3-bis(diphenylphosphino)calix[4]arene: Preparation, X-ray structures, and catalyses. *Organometallics* **2016**, *35*, 420-427.
- 402 30. Karpus, A.; Yesypenko, O.; Boiko, V.; Poli, R.; Daran, J.-C.; Voitenko, Z.; Kalchenko, V.; Manoury, E. Chiral  
403 phosphinoferrrocenyl-calixarenes. *Eur. J. Org. Chem.* **2016**, 3386-3394.
- 404 31. Kuhn, P.; Sémeril, D.; Jeunesse, C.; Matt, D.; Lutz, P. L.; Louis, R.; Neuburger, M. Catalytic applications of keto-stabilised  
405 phosphorus ylides based on a macrocyclic scaffold: calixarenes with one or two pendant Ni(P,O)-subunits as ethylene  
406 oligomerisation and polymerisation catalysts. *Dalton Trans.* **2006**, 3647-3659.
- 407 32. Frediani, M.; Sémeril, D.; Comucci, A.; Bettucci, L.; Frediani, P.; Rosi, L.; Matt, D.; Toupet, L.; Kaminsky, W.  
408 Ultrahigh-molecular-weight polyethylene by using a titanium calix[4]arene complex with high thermal stability under  
409 polymerization conditions. *Macromol. Chem. Phys.* **2007**, *208*, 938-945.
- 410 33. Walton, M. J.; Lancaster, S. J.; Redshaw, C. Highly selective and immortal magnesium calixarene complexes for the  
411 ring-opening polymerization of *rac*-Lactide. *ChemCatChem* **2014**, *6*, 1892-1898.
- 412 34. Sarkar, A.; Krishnamurthy, S. S.; Nethaji, M. Calix[4]arene bisphosphite ligands bearing two distal 2,20-biphenyldioxy or  
413 2,20-binaphthylidioxy moieties: Conformational flexibility and allyl-palladium complexes. *Tetrahedron* **2009**, *65*, 374-382.
- 414 35. Sémeril, D.; Matt, D.; Toupet, L.; Oberhauser, W.; Bianchini, C. High-pressure investigations under CO/H<sub>2</sub> of rhodium  
415 complexes containing hemispherical diphosphites. *Chem. Eur. J.* **2010**, *16*, 13843-13849.
- 416 36. Dieleman, C.; Steyer, S.; Jeunesse, C.; Matt, D. Diphosphines based on an inherently chiral calix[4]arene scaffold: Synthesis  
417 and use in enantioselective catalysis. *J. Chem. Soc., Dalton Trans.* **2001**, 2508-2517.
- 418 37. Karpus, A.; Yesypenko, O.; Boiko, V.; Daran, J.-C.; Voitenko, Z.; Kalchenko, V.; Manoury, E. Synthesis of an enantiomerically  
419 pure inherently chiral calix[4]arene phosphonic acid and its evaluation as an organocatalyst. *J. Org. Chem.* **2018**, *83*, 1146-1153.
- 420 38. Arnott, G. E. Inherently chiral calixarenes: Synthesis and applications. *Chem. Eur. J.* **2018**, *24*, 1744-1754.
- 421 39. Lejeune, M.; Sémeril, D.; Jeunesse, C.; Matt, D.; Lutz, P. J.; Toupet, L. Fast propene dimerization using upper  
422 rim-diphosphinated calix[4]arenes as chelators. *Adv. Synth. Catal.* **2006**, *348*, 881-886.
- 423 40. Monnereau, L.; Sémeril, D.; Matt, D.; Toupet, L.; Mota, A. J. Efficient, nickel-catalysed Kumada-Tamao-Corriu cross-coupling  
424 with a calix[4]arene-diphosphine ligand. *Adv. Synth. Catal.* **2009**, *351*, 1383-1389.
- 425 41. Monnereau, L.; Sémeril, D.; Matt, D.; Toupet, L. Cavity-shaped ligands: Calix[4]arene-based monophosphanes for fast  
426 Suzuki-Miyaura cross-coupling. *Chem. Eur. J.* **2010**, *16*, 9237-9247.

- 427 42. Sémeril, D.; Jeunesse, C.; Matt, D. Influence des propriétés intrinsèques de ligands calixaréniques sur des réactions de  
428 transformation catalytique de l'éthylène. *C. R. Chimie* **2008**, *11*, 583-594.
- 429 43. Lejeune, M.; Sémeril, D.; Jeunesse, C.; Matt, D.; Peruch, F.; Lutz, P. J.; Ricard, L. Diphosphines with expandable bite Angles:  
430 highly active ethylene dimerisation catalysts based on upper rim, distally diphosphinated calix[4]arenes. *Chem. Eur. J.* **2004**,  
431 *10*, 5354-5360.
- 432 44. Kuhn, P.; Jeunesse, C.; Sémeril, D.; D., M.; Lutz, P. J.; Welter, R.: Coordination chemistry of large diphosphanes directional  
433 properties of a calix[4]arene proximally substituted by two  $\text{OCH}_2\text{PPh}_2$  podand arms. *Eur. J. Inorg. Chem.* **2004**, 4602-4607.
- 434 45. Natarajan, N.; Pierrevet, M.-C.; Sémeril, D.; Bauder, C.; Matt, D.; Ramesh, R. Chiral calixarene and resorcinarene  
435 derivatives. Conical cavities substituted at their upper rim by two phosphito units and their use as ligands in Rh-catalysed  
436 hydroformylation. *Catal. Commun.* **2019**, *118*, 70-75.
- 437 46. Sémeril, D.; Jeunesse, C.; Matt, D.; Toupet, L. Regioselectivity with hemispherical chelators: Increasing the catalytic efficiency  
438 of complexes of diphosphanes with large bite angles. *Angew. Chem. Int. Ed.* **2006**, *45*, 5810-5814.
- 439 47. Gagnon, J.; Vézina, M.; Drouin, M.; Harvey, P. D. Regioselective upper-rim functionalizations of calix[4]arene by  
440 diphenylphosphino groups. *Can. J. Chem.* **2001**, *79*, 1439-1446.
- 441 48. Jaime, C.; de Mendoza, J.; Prados, P.; Nieto, P. M.; Sanchez, Carbon-13 NMR chemical shifts. A single rule to determine the  
442 conformation of calix[4]arenes. *C. J. Org. Chem.* **1991**, *56*, 3372-3376.
- 443 49. Liu, S.; Sandoval, C. A. Evaluation of calix[4]arene-based chiral diphosphite ligands in Rh-catalyzed asymmetric hydrogena-  
444 tion of simple dehydroamino acid derivatives. *J. Mol. Catal. A: Chem.*, **2010**, *325*, 65-72.
- 445 50. Diéguez, M.; Ruiz, A.; Claver, C. Chiral diphosphites derived from D-glucose: new highly modular ligands for the asymmet-  
446 ric catalytic hydrogenation. *J. Org. Chem.* **2002**, *67*, 3796-3801.
- 447 51. Kostas, I. D.; Vallianatou, K. A.; Holz, J.; Börner, A. Rhodium complexes with a new chiral nitrogencontaining BINOL-based  
448 diphosphite or phosphonite ligand: synthesis and application to hydroformylation of styrene and/or hydrogenation of  
449 prochiral olefins. *Appl. Organometal. Chem.* **2005**, *19*, 1090-1095.
- 450 52. Li, Y.; Ma, B.; He, Y.; Zhang, F.; Fan, Q.-H. Chiral metallacrown ethers for asymmetric hydrogenation: alkali-metal ion medi-  
451 ated enhancement of enantioselectivity. *Chem. Asian J.* **2010**, *5*, 2454-2458.
- 452 53. Cai, C.; Deng, F.; Sun, W.; Xia, C. New bidentate phosphorus ligands based on a norbornane backbone for rhodium-catalyzed  
453 asymmetric hydrogenation. *Synlett* **2007**, 3007-3010.
- 454 54. Chan, A. S. C.; Pluth, J. J.; Halpern, J. Identification of the enantioselective step in the asymmetric catalytic hydrogenation of a  
455 prochiral olefin. *J. Am. Chem. Soc.* **1980**, *102*, 5952-5954.
- 456 55. Halpern, J. Mechanism and stereoselectivity of asymmetric hydrogenation. *Science* **1982**, *217*, 401-407.
- 457 56. Landis, C. R.; Halpern, J. Asymmetric hydrogenation of methyl-(Z)- $\alpha$ -acetamidocinnamate catalyzed by  
458 {1,2-bis((phenyl-*o*-anisoyl)phosphino)ethane}rhodium(I): kinetics, mechanism, and origin of enantioselection. *J. Am. Chem. Soc.*  
459 **1987**, *109*, 1754-1757.
- 460 57. Sarkar, A.; Nethaji, M.; Krishnamurthy, S. K. Phosphite ligands derived from distally and proximally substituted dipropoxy  
461 calix[4]arenes and their palladium complexes: Solution dynamics, solid-state structures and catalysis. *J. Organomet. Chem.*  
462 **2008**, *693*, 2097-2110.
- 463 58. Liu, W.; Das, P. J.; Colquhoun, H. M.; Stoddart, J. F. Whither Second-Sphere Coordination? *CCS Chem.* **2022**, *4*, 755-784.