Diphosphite Ligands

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Regioselectivity with Hemispherical Chelators: Increasing the Catalytic Efficiency of Complexes of Diphosphanes with Large Bite Angles**

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The entrapment of substrates in molecular pockets that incorporate a metal ion constitutes an exciting approach to catalytic transformations displaying shape-, regio-, and enantioselectivity.[1–3] The environment of a bound substrate can be closely controlled by confinement of the metal center, in particular enabling a catalytic reaction to be driven towards the product that best adapts to the steric restraints imposed by the confining structure. Although these and other effects of coordination are seen to operate ubiquitously in biology, their transposition to catalytic systems of industrial relevance still remains limited.[4–8]

Calix[4]arenes are molecules readily fixed in various conformations that provide very different relative orientations of substituent groups. These substituent groups may contain donor atoms and the commonly encountered *cone* conformer thus provides not only a particularly useful plat-

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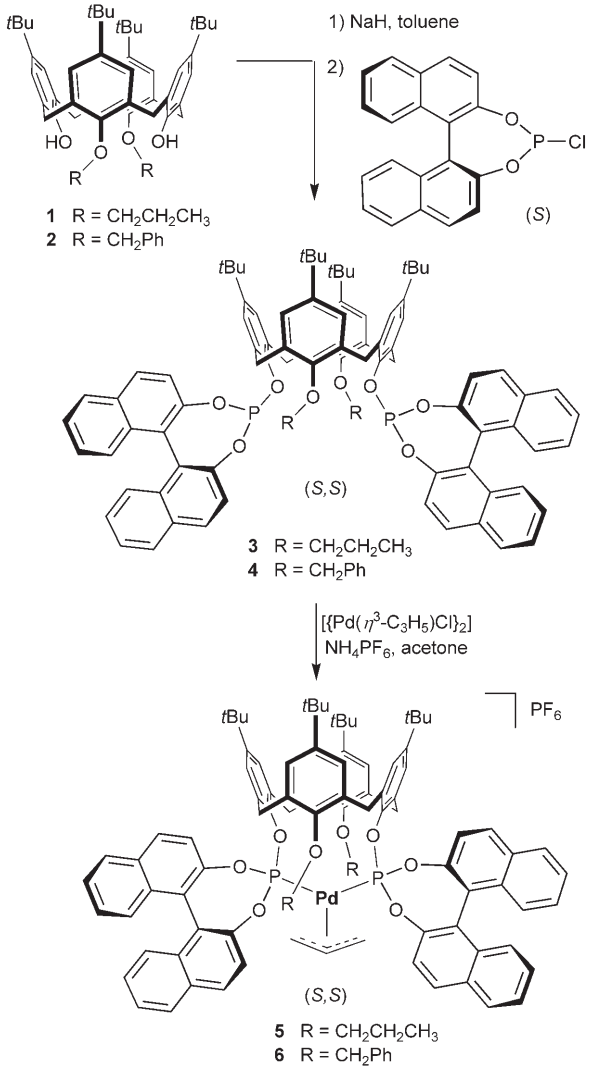
form for the construction of chelators with a constrained bite angle,[10] but also a convenient means of generating secondary coordination spheres.[9] We now report the synthesis and characterization of pocket-shaped, calixarene-based diphosphites that combine the advantage of an effective bite-angle control with that of steric pressure exerted, in the present case, by lateral pendent groups, anchored to two distal oxygen atoms of the macrocyclic skeleton. The catalytic activity of Pd^{II} and Rh^{I} complexes of these diphosphites has been evaluated in the allylic alkylation of unsymmetrical allyl acetates and in the hydroformylation of olefins.

Diphosphites **3** and **4** were prepared by double deprotonation of the corresponding dialkylated precursors **1** and **2**, respectively, followed by reaction with [(*S*)-(1,1′-binaphthalene-2,2′-diyl)]chlorophosphite (Scheme 1). The conical structure of the resulting calixarenes was unambiguously inferred from the ^{13}C NMR spectra, which both display $ArCH_2Ar$ signals near 32 ppm ($\delta = 31.96/33.30$ (**3**), 31.78/33.54 ppm (**4**)), that is, in a range typical for this conformation. In keeping with C_2 symmetry, the $ArCH_2$ protons of each ligand appear as two distinct AB patterns in the ^1H NMR spectrum, while the corresponding ^{31}P NMR spectra exhibit a single signal in the phosphite region ($\delta = 133.76$ (**3**), 123.59 ppm (**4**)). The rather large separation between the distal phenoxy rings of the calixarene moiety, combined with the steric bulk created by the "binaphthyl" moieties, makes these ligands, a priori, suitable for the synthesis of chelate complexes in which the P–M–P bite angle should significantly surpass 90°.

Complex **5** was obtained quantitatively by addition of one equivalent of **3** to a $[\{Pd(\eta^3\text{-allyl})Cl\}_2]/NH_4PF_6$ suspension in acetone. The formation of a chelate complex was inferred from the corresponding mass spectrum, which shows an intense peak at 1507.57, corresponding to the $[Pd(allyl)\cdot\mathbf{3}]^+$ cation. Owing to the presence of a η^3-bonded allyl ligand, the whole complex is no longer C_2 symmetrical. This is best seen in the ^1H NMR spectrum, which exhibits four AB systems for the $ArCH_2$ protons. The same features were observed for the related complex **6**, obtained in a similar way from **4**. As revealed by a single crystal X-ray diffraction study, diphosphite **3** displays a bite angle of ca. 107.5° in complex **5**. Obviously, the steric encumbrance of the binaphthyl units largely contributes to such a large bite angle (Figure 1), as in a related calixarene bearing significantly smaller $P(OR)_2$ moieties the P–M–P angle was found to be only 101°.[11] The molecular structure further shows that the metal–allyl moiety sits deep in a pocket generated by two nearly symmetrically sited naphthyl moieties and the two propoxy groups. We note also that, owing to the presence of a typically flattened cone conformation (Figure 1), the *O*-propyl groups are pushed towards the palladium center, and are therefore significantly involved in an effective embrace of the allyl group.



Scheme 1. Synthesis of the diphosphites and their cationic allyl–palladium complexes.

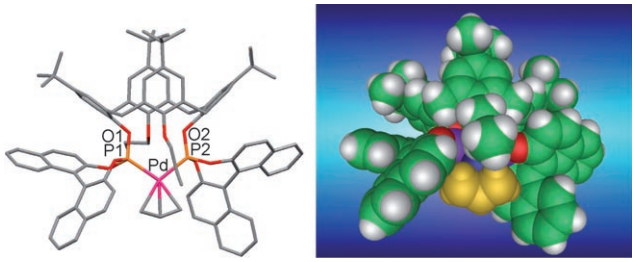
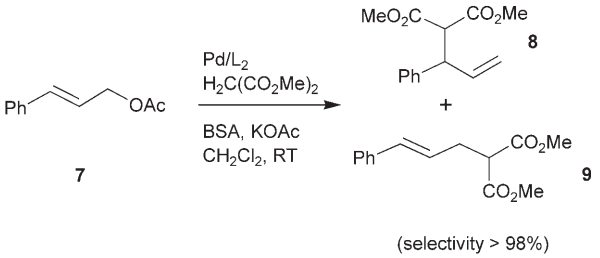
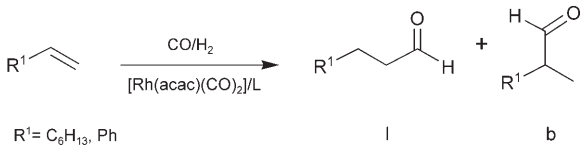


Figure 1. Molecular structure of **5**. In the CPK representation (right), the allyl group is in yellow. Selected bond lengths [Å] and angles [°]: Pd–P1 2.292(2), Pd–P2 2.294(2); P1–Pd–P2 107.50(8), O1–P1–Pd 119.6(2), O2–P2–Pd 119.3(2); interplanar angle between the two naphthyl moieties embracing the allyl group: 49.6°; dihedral angles between facing phenoxy rings: 81.1° (O1/O2), 2.0° (O3/O4). The PF_6 anion and the six CH_2Cl_2 solvent molecules are omitted for clarity.

The ligands **3** and **4** were assessed in the Pd-catalyzed alkylation of 3-phenylallyl acetate **7** with dimethyl malonate (Scheme 2). With both ligands, the linear product **9** was formed with over 98% selectivity (98.1% for **3**; 98.3% for **4**). This remarkably high regioselectivity sharply contrasts with that obtained for the same substrate using other diphosphanes.[12–16] Diphenylphosphanylethane (dppe), for example, led under similar conditions to a **9**:**8** ratio of 91.8:8.2. The highest linear:branched ratio obtained with a diphosphite,



Scheme 2. Palladium-catalyzed allylic substitution of the unsymmetrical substrate **7**. BSA = *N*,*O*-Bis(trimethylsilyl)acetamide.



Scheme 3. Rhodium-catalyzed hydroformylation of 1-octene and styrene. acac = acetylacetone.

93:7, was reported by Claver et al. for a furanoside diphosphite.[16] The unusual selectivities obtained with **3** and **4** might be explained by the presence of pockets created around the metal center. Molecular models clearly show that in the allyl complex formed with **7**, the unsubstituted allylic carbon atom is the one for which the incoming nucleophile interferes least with the naphthyl and *O*-alkyl groups, whatever the orientation of the phenylallyl group, *syn* or *anti*. It should be recalled here that steric parameters become particularly important in alkylation reactions that involve a late transition state. It is further interesting to note that, unlike the situation found in related Pd–allyl–Xantphos complexes,[17] the allyl embrace by the calixarene–diphosphites involves not only P substituents, but also auxiliary side groups axially positioned with respect to the metal center, hence resulting in an increased steric protection of the allyl moiety.

The homogeneous hydroformylation of olefins is the favorite application for diphosphanes with large bite angles.[5,18–23] The ligands **3** and **4** were therefore tested in the rhodium-catalyzed hydroformylation of *n*-octenes (Scheme 3). A large excess of phosphite was required to obtain high regioselectivities (compare entries 1 and 2 and 4 and 5 in Table 1), indicating relatively inefficient complexation and the possible involvement of a Rh catalyst species with only one or even no phosphite coordinated through its P atom.

Diphosphite **3**, bearing two pendant propoxy groups, turned out to be very effective for the hydroformylation of 1-octene. TOF values up to 1440 (Table 1, entry 2) were observed, for a l:b ratio as high as 58.0. We observed that the high preference for the linear product was maintained until the end of the reaction. Nevertheless, an important proportion of isomeric products was produced (ca. 50% of the amount of octene converted). This is possibly due to the steric encumbrance created about transient "Rh(isoalkyl)" moieties, which favors β elimination in these intermediates (and hence isomerization) over a carbonylation step. The ability of the Rh/**3** system to isomerize 1-octene led us to test **3** in the hydroformylation of the less reactive *trans*-2-octene. Here the TOF value droped to 170, but the selectivity towards the linear aldehyde remained good, the l:b ratio being kept in the range 4.3–4.6 (Table 1, entry 3). For comparison, using PPh_3[24] or van Leeuwen's most bulky Xantphite[25] gave l:b ratios of only 0.9 and 2.8, respectively.

The relevance of the pendent side groups for the regioselectivity was shown by replacing the propoxy substituents by the bulkier benzyloxy groups. Thus, in the hydroformylation of 1-octene with **4** at 80°C, the l:b ratio rose to 80 without loss of activity (Table 1, entry 5) and with little isomerization. When used in the hydroformylation of *trans*-2-octene at 120°C, **4** resulted in a high selectivity towards the linear aldehyde, the l:b ratio in this case reaching 24.9 (Table 1, entry 6). The latter result implies that under these conditions, isomerization towards 1-octene occurs.

Finally, the two diphosphites were assessed in the hydroformylation of styrene (Table 2, entries 1 and 3). In all catalytic runs, the linear aldehyde was the major product, whereas conventional mono- and diphosphanes usually give more branched product.[26] For example, at 20 bar, and after 20% conversion, the selectivity towards the linear aldehyde was 58.8% with **3** and 73.6% with the bulkier diphosphite **4**. Decreasing the pressure of CO/H_2 from 20 to 10 bar increased the selectivity to 67.4 (**3**) and 76.1% (**4**), respectively, without reducing significantly the activity (Table 2, entries 2 and 4). This unusual regioselectivity can, in line with van Leeuwen's findings made for ligands with large bite angles, be assigned to a pocket effect. The fact that the selectivity of **4** towards the linear aldehyde is higher than that of the propoxy-substituted ligand **3** is of course a clear indication that the degree of steric

Table 1: Rhodium-catalyzed hydroformylation of *n*-octenes using diphosphites **3** and **4**.

Entry	Olefin	Ligand	L/Rh	*t* [h]	Conversion [%][a]	TOF[b]	l:b[c]	Isomerization [%][d]
1[e]	1-octene	**3**	1	3.75	32.1	430	3.2	9.6
2[e]	1-octene	**3**	10	1.2	34.5	1440	58.0	17.0
				8	98.5	620	56.3	46.7
3[f]	*trans*-2-octene	**3**	10	2	41.6	170	4.3	1.9
				8	70.0	70	4.6	3.4
4[e]	1-octene	**4**	1	1	23.1	1150	7.2	2.6
5[e]	1-octene	**4**	10	1	23.9	1190	n.d.[g]	3.0
				24	87.3	180	80.1	12.1
6[f]	*trans*-2-octene	**4**	10	8	44.6	50	24.9	3.3

[a] Determined by GC; calibration based on decane. [b] mol(converted octene) per mol(Rh) and hour. [c] Ratio, percent of linear (l) aldehyde to percent of branched (b) aldehyde. [d] Isomerized 1-octene/all octenes or 2-octene/all octenes. [e] Reaction conditions: 1-octene (10 mmol), 1-octene/Rh = 5000, initial pressure (at 80°C): 20 bar CO/H_2 (1/1), T = 80°C, toluene/*n*-decane (15 mL/0.5 mL), incubation overnight at 80°C. [f] Reaction conditions: *trans*-2-octene (3.2 mmol), *trans*-2-octene/Rh = 800, initial pressure (at 120°C): 20 bar CO/H_2 (1/1), T = 120°C, toluene/*n*-decane (15 mL/0.5 mL), incubation overnight at 80°C. [g] Not determined, because of a very low amount of branched aldehyde.

Table 2: Rhodium-catalyzed hydroformylation of styrene using diphosphites **3** and **4**.[a]

Entry	Ligand	$p(CO/H_2)$ [bar]	t [h]	Conversion [%][b]	TOF[c]	Branched [%]	Linear [%]
1	**3**	20	5	18.3	180	41.2	58.8
2	**3**	10	5	21.7	220	34.8	65.2
			24	58.7	120	32.6	67.4
3	**4**	20	4.5	19.1	210	26.4	73.6
4	**4**	10	5.5	21.4	200	23.9	76.1
			24	64.4	134	23.4	76.6

[a] Reaction conditions: styrene (10 mmol), styrene/Rh = 5000, L/Rh = 10, CO/H_2 (1/1) initial pressure (at 80 °C), T = 80 °C, toluene/*n*-decane (15 mL/0.5 mL), incubation overnight. [b] Determined by GC, calibration based on decane. [c] mol(converted styrene) per mol(Rh) and h.

protection about the metal center plays a key role for the catalytic outcome. This is also in keeping with the observation that the selectivity obtained with **4** is somewhat better than that reported for the Xantphites, which have similar large bite angles, but which are deprived of any side group able to exert an additional steric pressure on the first coordination sphere of the metal.[25]

Overall, calixarenes **3** and **4** provide unprecedented examples of hemispherical chelators able to drive allylic alkylation as well as olefin hydroformylation reactions towards the formation of "linear" products. With these ligands, the metal embrace is particularly effective, the large bite angles being associated with a conformation of the calixarene which produces a steric protection by the *O*-alkyl substituents of the apical positions on the metal, already encumbered by the substituents on the bound P atoms. These steric effects are cooperative consequences of the known fact that flattening of the orientation of two opposed phenyl rings of a calix[4]arene to the mean macrocyclic plane results in a steeper orientation of the other pair.

Experimental Section

Full experimental details for all products are given in the Supporting Information.

3: ^{1}H NMR (300 MHz, C_6D_6): δ = 7.69–7.27 (15 H, CH_{arom}), 7.18–6.98 (10 H, CH_{arom}), 6.95–6.75 (7 H, CH_{arom}), 5.10 and 3.52 (AB system, 4 H, $ArCH_2Ar$, ^2J = 13.0 Hz), 5.00 and 3.00 (AB system, 4 H, $ArCH_2Ar$, ^2J = 13.0 Hz), 4.00–3.79 (m, 4 H, OCH_2), 2.06–1.85 (m, 4 H, CH_2CH_3), 1.26 (s, 18 H, $C(CH_3)_3$), 1.23 (s, 18 H, $C(CH_3)_3$), 0.39 ppm (t, 6 H, CH_2CH_3, ^3J = 7.4 Hz). $^{13}C\{^1H\}$ NMR (75 MHz, C_6D_6): δ = 154.10–121.98 (C_{arom}), 77.34 (s, OCH_2), 33.81 (s, $C(CH_3)_3$), 33.79 (s, $C(CH_3)_3$), 33.30 (s, $ArCH_2Ar$), 31.96 (s, $ArCH_2Ar$), 31.43 (s, $C(CH_3)_3$), 31.40 (s, $C(CH_3)_3$), 22.96 (s, CH_2CH_3), 9.44 ppm (s, CH_2CH_3). $^{31}P\{^1H\}$ NMR (121 MHz, C_6D_6): δ = 133.76 ppm (s, $OP(OAr)_2$).

Crystal structure of **5**·6 CH_2Cl_2: M_r = 2163.56, monoclinic, $P2_1$, a = 13.4071(7), b = 23.4689(8), c = 17.0844(8) Å, β = 102.469(4)°, V = 5248.8(4) Å^3, Z = 2, D_x = 1.369 mg m^{-3}, $\lambda(Mo_{K\alpha})$ = 0.71073 Å, μ = 5.91 cm^{-1}, $F(000)$ = 2228, T = 100(1) K. Data were collected on an Oxford Diffraction Xcalibur Saphir 3 diffractometer (graphite $Mo_{K\alpha}$ radiation, λ = 0.71073 Å). The structure was solved with SIR-97[27] which revealed the non-hydrogen atoms of the molecule. After anisotropic refinement, many hydrogen atoms were found with a Fourier difference analysis. The whole structure was refined with SHELX-97[28] and full-matrix least-square techniques (use of F^2; x, y, z, β_{ij} for Pd, P, F, Cl, C and O atoms, x, y, z in riding mode for H atoms; 1163 variables and 11795 observations with $I > 2.0\,\sigma(I)$; calc $w = 1/[\sigma^2(F_o^2) + (0.18P)^2 + 28.7P]$ where $P = (F_o^2 + 2F_c^2)/3$. R = 0.088, R_w = 0.248, S_w = 0.938, $\Delta\rho < 2.9$ e Å^{-3}. CCDC 297616 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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