Multifunctional Calixarene-derived Phosphinites

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The syntheses of unprecedented di and tri-functional phosphinites derived from *p-tert*-butylcalix[4]arene are described.

Multidentate phosphorus(III) compounds play a major role both in coordination chemistry and catalysis.[1] Since the first publications on simple bidentate or tridentate P^{III} ligands such as $Ph_2PCH_2CH_2PPh_2$ or $PhP(CH_2CH_2PPh_2)_2$, an impressive number of tailor-made multidentate phosphorus containing ligands have been reported.[2] The ligand properties of these molecules strongly depend on the nature of the spacers which separate the individual tricoordinate phosphorus atoms. It is in particular expected that the geometry and the rigidity of these bridging units determine the shape of coordination spheres and therefore, at least partially, the properties of the resulting complexes.

p-tert-Butylcalix[4]arenes are cyclic tetramers which may exist in four conformation types built around cavity shaped architectures, the cone conformation being the most frequently encountered.[3] Owing to the presence of four phenolic moieties, these molecules are potential precursors of a variety of 'heterofunctionalized' multidentate transition metal ligands. Thus, the anchoring of hard and soft binding sites on a pre-organizing cyclic tetraphenol matrix could be of particular interest for the study of anchimeric assistance[4] in transition metal centred reactions. The spontaneous ability of calixarenes to retain solvent molecules may furthermore be helpful in the control of ligand bite angles and therefore confer additional stability to metal complexes. Despite the relevance of phosphinites for transition metal catalysis,[5] only two phosphinites derived from *p-tert*-butylcalix[4]arene 1 have been reported to date.[6,7] In this preliminary communication
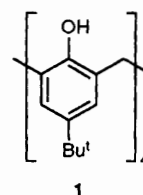

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Table 1

Compound	MS[a]	IR[b] $\nu_{C=O}$/cm^{-1}	^{31}P{^{1}H} NMR[c] δ_P	^{1}H NMR[d] δ_{HA}, δ_{HB} of ArCH_2	^{13}C NMR[e] δ_C of ArCH_2
3	1005	1762, 1734	122.9	3.16, 4.59/3.33, 4.96	31.29, 31.40
4	1189	1762	123.2	2.84, 4.39	32.52
8	1131	1761	123.2	2.77, 4.10/2.87, 4.45	31.80, 32.76
9	1273^f	1759	123.7, 123.8	2.76, 4.07 or 4.11/ 2.82, 4.07 or 4.11/ 2.85, 4.40/2.85, 4.42	32.03, 32.08, 32.65, 32.70
11	1045	—	120.3	2.89, 3.87^g	32.79
12	1045	—	113.6	2.50, 3.50/3.68, 4.06^h	29.25, 38.81^h

a By CI except for compound **12** (FAB$^+$). *b* KBr pellets. *c* In THF–[^{2}H$_6$]benzene. *d* In CDCl$_3$ except for compound **3** in [^{2}H$_6$]benzene; 200 MHz spectra, except for **9**, 400 MHz. *e* In CDCl$_3$. *f* Corresponds to M + H$^+$ + 2 O. *g* Measured at 25 °C. *h* Measured at −30 °C.
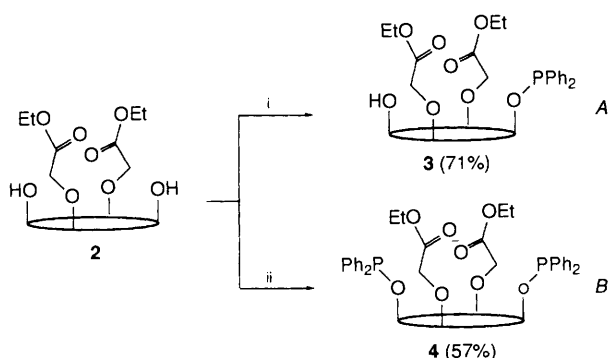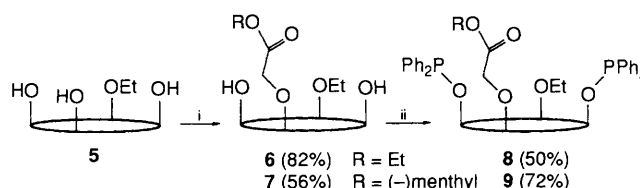

Scheme 1 *Reagents and conditions*: i, a, NEt$_3$ (2.5 equiv.), −40 °C, THF; b, Ph$_2$PCl (1 equiv.), −40 °C; c, reflux 36 h; ii, a, LiNPr$^i_2$ (2 equiv.), −78 °C, THF; b, Ph$_2$PCl (2 equiv. in THF), −78 °C

Scheme 2 *Reagents and conditions*: i, a, K$_2$CO$_3$ (0.6 equiv.); b, BrCH$_2$CO$_2$R (1.2 equiv.), 15 h reflux in MeCN; ii, a, LiNPr$^i_2$ (2 equiv.) in THF, −78 °C; b, Ph$_2$PCl (2 equiv.) in THF, −78 °C

we report the synthesis and properties of a series of new hybrid phosphinites derived from **1**.

All ligands described here were prepared from precursors with a cone conformation. In each case the key step is the deprotonation of one or two phenol moieties followed by reaction with diphenylchlorophosphine. The phosphinites **3** and **4** were prepared in two steps respectively according to *A* and *B* (Scheme 1): reaction of the diester **2**[8] with a large excess of NEt$_3$ (2.5 equiv.) in tetrahydrofuran (THF) and subsequent addition of Ph$_2$PCl (1 equiv.) gave selectively the monophosphinite compound **3** as a white powder. All attempts to introduce a second Ph$_2$P group using NEt$_3$ were unsuccessful; the formation of the bis-phosphinite **4** requires the use of a strong base such as LiNPr$^i_2$.† Compounds **3** and **4** were characterized by ^{1}H, ^{31}P and ^{13}C NMR and IR spectroscopy, elemental analysis and mass spectrometry (Table 1). The ^{31}P{^{1}H}NMR spectrum of both compounds shows a typical phosphinite signal at δ 123. It is noteworthy that for compound **3** a $^5J_{P-ArCH_2}$ coupling constant of 2 Hz could be detected in the ^{1}H NMR (CDCl$_3$, 200 MHz, −30 °C) spectrum between the phosphorus atom and one of the two ArCH$_2$Ar protons of the neighbouring methylene groups. Compounds **3** and **4** are in a cone conformation as deduced from following data: (*i*) the ^{13}C chemical shifts of the ArCH$_2$Ar carbon atoms are typical for a *syn*[9] arrangement of the geminal aryl groups;[10] (*ii*) for all ArCH$_2$Ar methylene groups, the difference of chemical shifts between the non-equivalent methylene protons lies in the range usually found for cone conformations.[3a,11]

The trifunctional phosphinite ligands **8** and **9** were both prepared in two steps from the readily available ethoxy
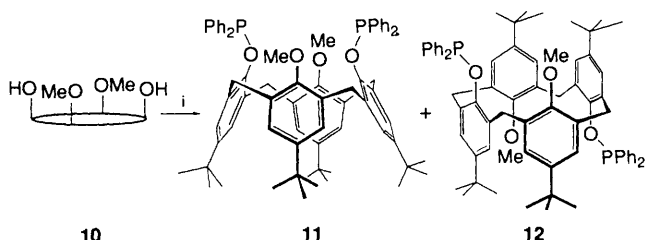
derivative **5**[12] (Scheme 2). Introduction of a single CH$_2$C(O)OR group into **5** [R = C$_2$H$_5$ or (−)-menthyl] was achieved by reaction in acetonitrile with K$_2$CO$_3$ and the corresponding bromoacetate to give **6** and **7**.‡ The ^{1}H and ^{13}C NMR data of these intermediates are consistent with cone conformations. Reaction of **6** and **7** with LiNPr$^i_2$, followed by reaction with Ph$_2$PCl yielded respectively compounds **8** and **9**. Important characterizing data are given in Table 1. As can unambigously be deduced from the ^{1}H and ^{13}C NMR data, no conformational change is to be observed on going from **6** to **8** or **7** to **9**. The ^{31}P NMR chemical shift values of **8** and **9** fall in the expected range. Owing to the absence of any symmetry element in the chiral bis-phosphinite **9**, the two phosphorus

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† The yields indicated in reactions *A* and *B* are isolated yields. Owing to the extremely high solubility of **3** and **4** in usual organic solvents, the precipitation of these compounds from the reaction mixtures was always incomplete. Whereas the reaction *A* shown is selective, that of *B* leads to, besides **4**, some unidentified products which were detected in the residual mother liquor.

‡ *Selected spectroscopic data* for **6**: MS (FAB): 762.4 (M$^+$, 100%). IR(KBr) ν/cm^{-1}: 3458br, 1756br (C=O). ^{1}H NMR (CDCl$_3$): δ 0.92 (s, 9H, Bu^t), 0.99 (s, 9H, Bu^t), 1.29 (s, 18H, Bu^t), 1.36 (t, 3H, CH$_2$CH_3, ^3J 7.1 Hz), 1.60 (t, 3H, CH$_2$CH_3, ^3J 7.1 Hz), 3.32 and 4.44 [AB spin system, 4H, ArCH$_2$Ar, J_{AB} 13.1 Hz], 3.32 and 4.28 (AB spin system, 4H, ArCH$_2$Ar, J_{AB} 13.1 Hz), 4.10 (q, 2H, CH_2CH$_3$, ^3J 7.1 Hz), 4.32 (q, 2H, CH_2CH$_3$, ^3J 7.1 Hz), 4.68 (s, 2H, OCH$_2$CO$_2$Et), 6.75 (s, 2H, *m*-ArH), 6.83 (s, 2H, *m*-ArH), 7.05 (s, 4H, *m*-ArH), 7.24 (s, 2H, OH). ^{13}C{^{1}H} NMR (CDCl$_3$): δ 14.25 (s, CH$_2$CH_3), 15.43 (s, CH$_2$CH_3), 31.06 [s, C(CH_3)$_3$], 31.13 [s, C(CH_3)$_3$], 31.77 [s, C(CH_3)$_3$], 31.86 (s, ArCH_2Ar), 31.93 (s, ArCH_2Ar), 33.90 [s, C(CH$_3$)$_3$], 33.99 [s, C(CH$_3$)$_3$], 61.26 [s, C(O)OCH_2CH$_3$], 72.14 (s, OCH_2, not assigned), 72.60 (s, OCH$_2$, not assigned), 125.06 (s, aromatic CH), 125.23 (s, aromatic CH), 125.53 (s, aromatic CH), 125.76 (s, aromatic CH), 127.87–150.87 (aromatic C$_{quat}$), 169.17 (s, C=O).

7: MS (FAB): 873.5 (M + H$^+$), 872.5 (M$^+$, 100%). IR (KBr) ν/cm^{-1}: 3462m (OH), 1757s and 1735s (C=O). ^{1}H NMR (CDCl$_3$): δ 0.77–2.13 (18H, menthyl), 0.94 (s, 9H, Bu^t), 1.00 (s, 9H, Bu^t), 1.29 (s, 18H, Bu^{t}ArOH), 1.60 (t, 3H, CH$_2$CH_3, ^3J 7.1 Hz), 3.32 and 4.28 (AB spin system, 2H, ArCH$_2$Ar, J_{AB} 13 Hz), 3.32 and 4.30 (AB spin system, 2H, ArCH$_2$Ar, J_{AB} 13 Hz), 3.32 and 4.46 (AB spin system, 2H, ArCH$_2$Ar, J_{AB} 13 Hz), 3.32 and 4.48 (AB spin system, 2H, ArCH$_2$Ar, J_{AB} = 13 Hz), 4.66 and 4.76 [AB spin system, 2H,OCH$_2$C(O)Omenth, J_{AB} 15.8 Hz], 4.88 (dt, 1H, OCH of menth, ^3J 4.4, ^3J 10.8 Hz), 6.76 (s, 2H, *m*-ArH), 6.84 (s, 2H, *m*-ArH), 7.04 (s br, 4H, *m*-ArH), 7.25 (s, 1H, OH), 7.28 (s, 1H, OH). ^{13}C{^{1}H} NMR (CDCl$_3$): signals of the menthyl group: δ 14.27, 19.61, 20.83, 22.44 (s, CH$_2$), 25.20, 30.35, 33.12 (s, CH$_2$), 39.74 (s, CH$_2$), 45.86, 74.30 (s, OCH); other signals: δ 15.28 (s, OCH$_2$CH_3), 29.86 [s, C(CH_3)$_3$], 29.95 [s, C(CH_3)$_3$], 30.58 [s, C(CH_3)$_3$], 30.74 (s br, ArCH$_2$Ar), 32.70 [s, C(CH$_3$)$_3$], 32.80 [s, C(CH$_3$)$_3$], 70.87 (s, OCH_2), 71.44 (s, OCH_2), 124.04 (s, aromatic CH), 124.29 (s, aromatic CH), 124.34 (s, aromatic CH), 124.49 (s, aromatic CH), 126.73–149.93 (12 s, aromatic C$_{quat}$), 169.69 (s, C=O).

10　　　　　**11**　　　　　**12**

Scheme 3 *Reagents and conditions*: i, a, Bu^{n}Li–hexane (2 equiv.), THF, room temp.; b, Ph$_2$PCl (2 equiv.), 0 °C, THF; c, reflux, 4 h
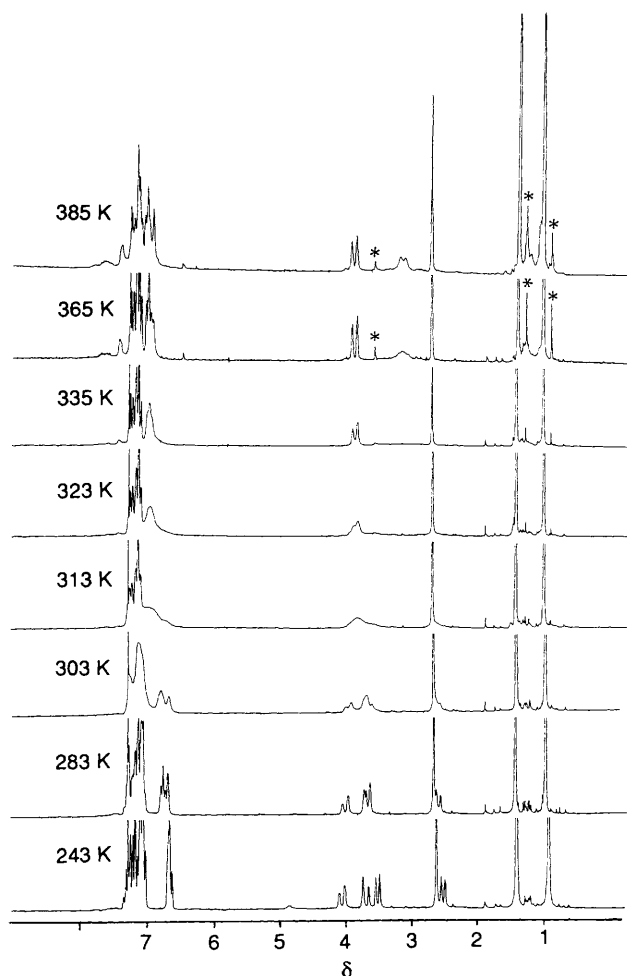

Fig. 1. Variable ^{1}H NMR spectrum of the 1,2-alternate conformer **12** (CDCl$_3$, 200 MHz, sealed tube). The asterisk indicates a decomposition product appearing after prolonged heating.

atoms appear as two distinct signals in its ^{31}P NMR spectrum (peak separation: *ca.* 0.1 ppm).

Whereas the reactions shown in Schemes 1 and 2 lead to calixarene-derived phosphinites with cone conformation, the situation changes when the starting compound is the cone dimethoxy compound **10**.[13] Sequential reaction of **10** with Bu^{n}Li (2 equiv.) and then with Ph$_2$PCl (2 equiv.) gave a mixture of the bis-dimethoxy, bis-phosphinite isomers **11** (yield 25%) and **12** (yield 60%), adopting respectively a cone and a 1,2-alternate conformation (Scheme 3). When performing this reaction at −78 °C, compound **11**§ could selectively be obtained in 82% yield. The assignment of a 1,2-alternate conformation of **12** can be made on the basis of the following data: the ^{1}H NMR spectrum, measured at −30 °C, shows a

§ A careful examination of the NMR spectra (200 MHz, CDCl$_3$) of compound **11** shows that this compound displays dynamic behaviour in solution: on lowering the temperature the signals gradually broaden, coalesce at *ca.* 260 K and become again sharp at lower temperatures, giving a set of signals which could not be interpreted.

singlet for the six methoxy protons, two 1 : 1 singlets for the Bu^t groups and two distinct (1 : 1) ArCH^{A}H^B spin systems. The ^{31}P{^{1}H}NMR spectrum shows a single peak at δ 113.6. Compound **12** displays dynamic behaviour in solution. As shown by a variable temperature study (Fig. 1), the signals of each of the two ArCH^{A}H^B spin systems broaden on rising the temperature, coalesce and finally converge to a single average AB spin system. These results unambiguously demonstrate a rapid interconversion between two opposite 1,2-alternate topomers. To the best of our knowledge, this constitutes the first example of homomerization of 1,2-alternate conformers. Whether this transformation results from a stepwise or a simultaneous rocking of the two aryl-methoxy units cannot be answered at the moment. THF solutions of **11** and **12** are stable on standing for several days. Interestingly, the reaction of Scheme 3 contrasts with the recent results of Moran and Roundhill[7] who found that treatment of **10** with KH (2 equiv.) followed by reaction with Ph$_2$PCl (2 equiv.) selectively yields a rigid isomer of **11** having a partial cone conformation. This emphasizes the role of the nature of the deprotonation agent used in the synthesis of a given conformer. In subsequent papers, the coordination properties of the herein reported phosphinite ligands will be described.

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