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Synthesis, separation and configurational analysis of phosphonated and partially phosphonated cavitands derived from resorcinarenes are described. The configuration of all diastereomers has been elucidated by their ¹H, ³¹P NMR spectra and ¹³C relaxation times. In all cases the course of the bridging reaction favours the formation of the sterically more crowded stereoisomers having the P=O groups oriented outward with respect to the cavity.

Introduction

We recently reported the synthesis of different diastereomeric cavitands by incorporation of four phosphate groups on resorcinarene molecular platforms.^{1,2} The reaction led to all the six possible diastereomers having different orientation of the P=O groups either inward (i) or outward (o) with respect to the cavity. Since the desired **iii** and **iiio** isomers, having respectively four and three convergent P=O groups capable of multiple hydrogen-bonding interactions, were synthesised in minor amounts, we needed a more selective synthesis. The approach chosen required the preparation of phosphonate cavitands, obtained by reaction of resorcinarenes with phenylphosphonic dichloride. The absence of the oxygen connecting the phosphorus to the phenyl group prevents the substituents from assuming an upward orientation with respect to the cavity, which was assumed to be the reason for the lack of selectivity. Examination of the CPK models revealed that the resulting cavitands could easily accommodate only one phenyl substituent pointing inwards, thus favouring the **iiio** and **iii** diastereomers over

the others. To our surprise the stereochemical outcome of the reaction was completely different. At the same time a paper appeared in the literature, that reported the selective synthesis of the **iii** isomer of a phenylphosphonate resorcinarene.³ This prompted us to undertake a detailed study into the reaction between resorcinarenes and phenylphosphonic dichloride.

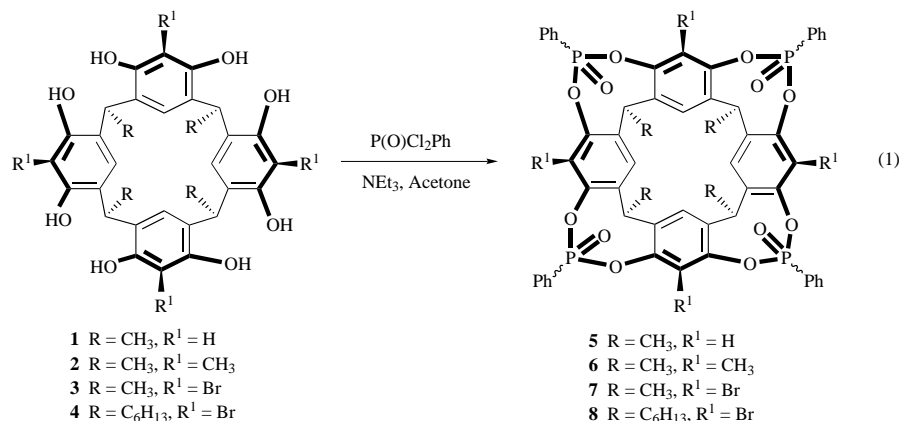
Results and discussion

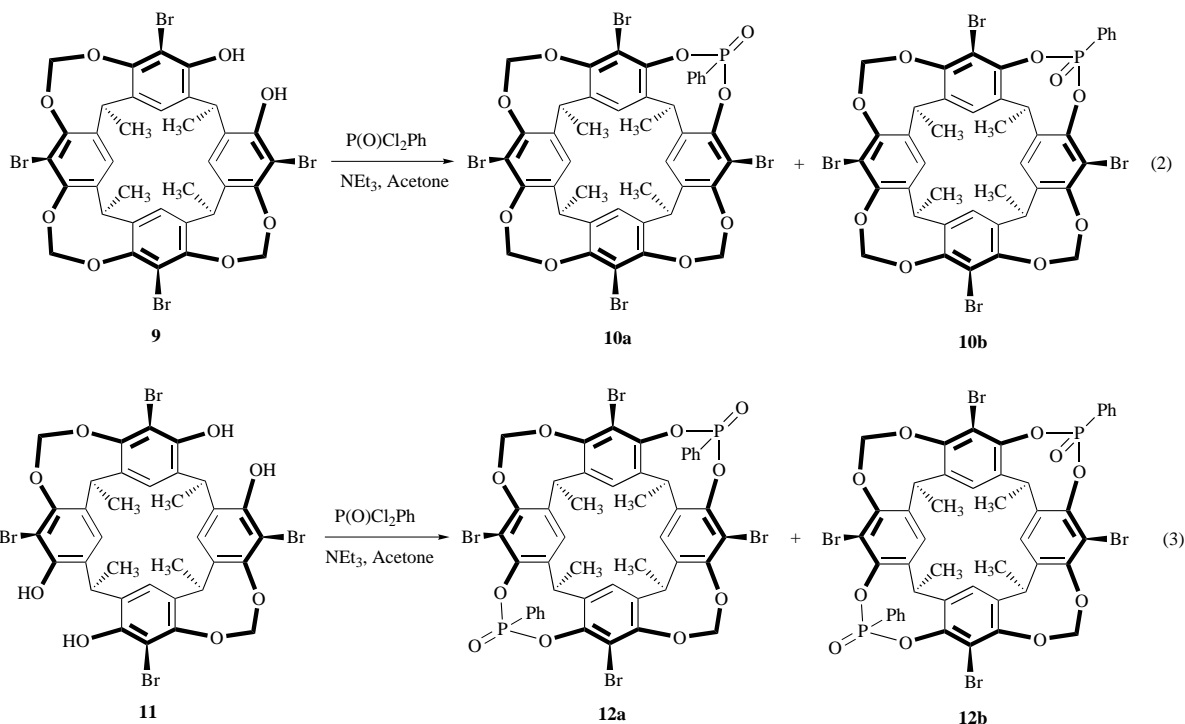
Synthesis and separation

Resorcinarenes **1–4** were used as molecular building blocks for the preparation of the tetraphosphonate cavitands **5–8** [reaction (1)]. All-*cis*-tetramethylresorcinarenes **1** and **2** were prepared from the corresponding resorcinols and acetaldehyde under acidic conditions.⁴ The tetrabromo derivatives **3** and **4** were obtained by reaction of the corresponding resorcinarenes using *N*-bromosuccinimide. The bridging reaction was carried out with dichlorophenylphosphonate using triethylamine as base in dry acetone: 30–50% overall yields were achieved in all cases. The products were diastereomeric mixtures in which at least three of the six possible isomers were present. Analogous reactions on the tri-bridged resorcinarene **9**⁵ and A,C-methylene-di-bridged **11**⁶ led to the isolation of **10a,b** and **12a,b** respectively [reactions (2) and (3)]. All isomers were separated and characterized (see Experimental section).⁷

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Configurational analysis

The reaction of resorcinarene **1** with phenylphosphonic dichloride led to the formation of four different diastereomers out of the six theoretically possible (Fig. 1). Of these isomers only **5a** presents a ^1H NMR spectrum compatible with C_{4v} symmetry structure, diagnostic of either the **iiii** or **oooo** isomers. Contrary to what was expected on the basis of CPK models, which predicted a highly crowded cavity for the **oooo** isomer, the chemical shifts of the R^2 protons were shifted upfield, strongly supporting the **oooo** structure. In order to investigate the stereochemical outcome of this reaction, we simplified the system by introduction of a single phenylphosphonic unit on resorcinarene **9**. In this case the reaction gave rise to both possible diastereomers **10a** (o isomer) and **10b** (i isomer) in a 2:1 ratio [reaction (2)]. The unequivocal assignment of the two isomers has been given on the basis of the following experimental data: (i) the R^2 protons directed into the cavity exhibit a remarkable upfield shift (6.82 ppm for the *ortho* protons of the o isomer and 8.29 ppm for those of the i isomer); (ii) phosphorous atoms bearing R^2 groups directed into the cavity have resonances at higher fields with respect to those with R^2 groups directed outward (7.56 ppm for **10a** and 8.84 ppm for **10b**); (iii) the spectral multiplicity of the methine present in the rigid eight-membered dioxaphosphocino ring: in **10b** (i isomer) this proton shows a coupling constant with ^{31}P of 2.4 Hz absent for **10a** (o isomer). From the literature it is known that in cyclic phosphonates the J_{HP} value depends on the relative orientation of the hydrogen with respect to the $\text{P}=\text{O}$ group: when the groups are *anti* (i isomer) the J_{HP} value is significantly higher than in the case of a *syn* orientation (o isomer).⁸

We then moved to the introduction of two distal phenylphosphonic units on resorcinarene **11**. The reaction led to the isolation of only two of the three possible diastereomers: **12a** (oo isomer) and **12b** (io isomer) as major component [reaction (3)]. The **ii** isomer was not detected. The identification of the two diastereomers was accomplished on the basis of the same spectroscopic proofs given for compound **10a,b** (see Experimental section). The product distribution obtained by the reaction of partially bridged resorcinarenes indicates a preference for the inward orientation of the phenyl groups.

We then studied the reaction of resorcinarenes **1–4** with phenylphosphonic dichloride [reaction (1)]. For all compounds

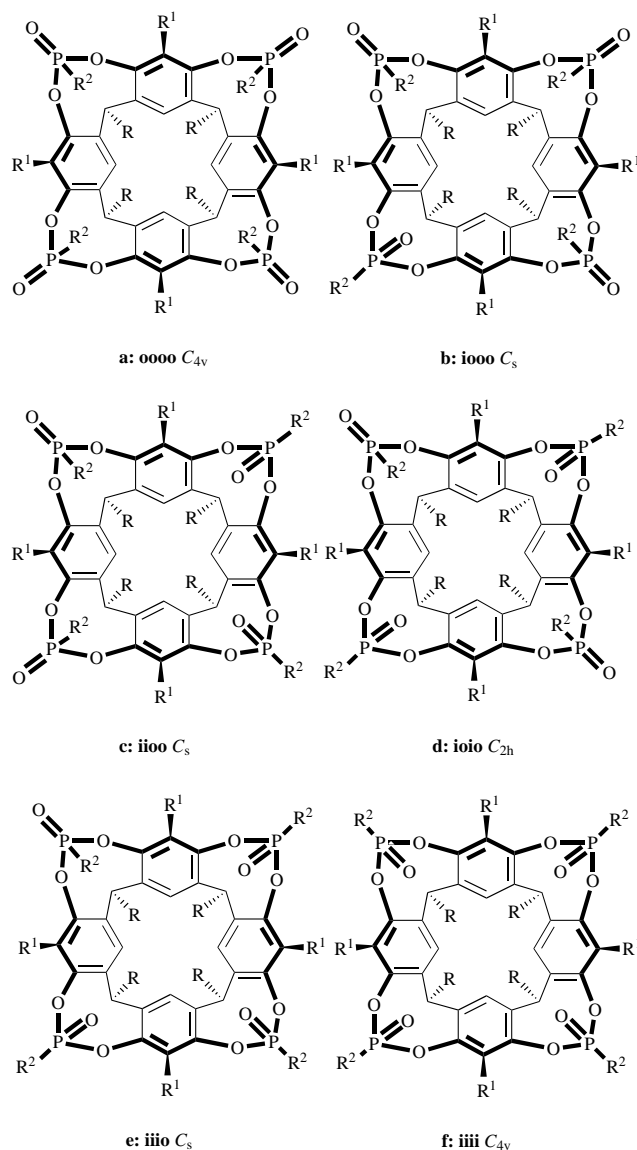


Fig. 1 The six possible diastereomers of phosphonate cavitands

Table 1 ^1H NMR chemical shifts and multiplicity of the methine protons of the resorcinarene skeleton of **5–8** in CDCl_3 at 25 °C

Compound	oooo		iooo		iioo		ioio	
	δ_{H}	Mult.	δ_{H}	Mult.	δ_{H}	Mult.	δ_{H}	Mult.
5	5.24(4)	q	5.02(1)	dq	5.04(2)	dq	5.05(2)	dq
			5.18(1)	q	5.23(2)	q	5.48(2)	q
			5.29(2)	q				
			5.00(1)	dq	5.02(2)	dq		
6	5.27(4)	q	5.13(1)	q	5.15(2)	q	—	—
			5.27(2)	q				
			—	—	5.02(2)	dq	5.05(2)	dq
			—	—	5.54(2)	q	5.48(2)	q
7	—	—	4.75(1)	dt	4.79(2)	dt	4.72(2)	dt
			5.13(1)	t	5.20(2)	t	5.26(2)	t
			5.27(2)	t				

Table 2 ^{31}P NMR chemical shifts of **5–8** in CDCl_3 at 25 °C

Compound	δ_{P}			
	oooo	iooo	iioo	ioio
5	9.0(4)	9.3(2)	7.6(2)	9.0(2)
		9.6(1)	10.3(2)	9.9(2)
		10.9(1)		
		5.3(2)	3.6(2)	—
6	5.9(4)	7.0(1)	9.1(2)	—
		9.9(1)		
		—	6.6(2)	6.6(2)
7	—	—	9.2(2)	9.2(2)
		—	5.0(2)	4.8(2)
8	—	8.7(2)	9.3(2)	9.4(2)
		9.9(1)		
		10.3(1)		

Table 3 Isomer distribution of cavitands **5–8** obtained by column chromatography separation

Compound	R^1	Overall isolated yield (%)	Isomers			
			a oooo	b iooo	c iioo	d ioio
5	H	50	3	31	10	6
6	CH_3	30	2	15	8	5
7	Br	35	—	—	7	28
8	Br	44	—	10	26	8

the signal patterns expected for the symmetry of the different isomers were in agreement with the experimental data of ^1H and ^{31}P NMR spectroscopy. The number of resonances of the phosphorous atoms and CH protons of the resorcinarene bridges are an indication for the different symmetries of the separated diastereomers (Table 1 and Table 2). Combination of these data allowed the unequivocal identification of isomers **c** (iioo; C_s) and **d** (ioio; C_{2h}) for compounds **5–8**. Identification of the remaining isomers requires the same considerations given for **10a,b**. These data led to the attribution of the iioo configuration for the **b** isomers (C_s) and the oooo configuration for the **a** ones (C_{4v}). In fact, for the **b** isomers the ^1H NMR spectrum shows predominantly high field R^2 signals and only one CH proton coupled with the ^{31}P ($J_{\text{HP}} = 2.0$ Hz); for the **a** isomers all the R^2 signals are shifted upfield and the CH protons are not coupled with the phosphorous atom.

The observed diastereomeric distribution for **5–8** is reported in Table 3. In all cases it deviates significantly from the theoretical statistical distribution (**a**:**b**:**c**:**d**:**e**:**f** = 1:4:4:2:4:1), towards the formation of predominantly **a** isomers. Variation of the R^1 groups in the apical position of the resorcinarene skeleton does not significantly change the isomer distribution. Increasing the bulkiness of the R^1 substituents by introducing bromine in **7**, disfavours the oooo and the iioo isomers. Since in

Table 4 ^1H NMR chemical shifts of the aromatic region of cavitand **8c**

δ_{H}	Intensity	Multiplicity
8.22	4	dd
7.66	2	t
7.54	4	m
7.41	2	t
7.31 + 7.36	4	s + s
7.13	4	m
7.06	4	m

this case solubility problems were encountered, the same reaction was performed on the more soluble resorcinarene **4** having C_6 alkyl chains. The results confirmed the absence of the oooo isomer, while the iioo could be isolated and characterized. In general, the introduction of four phenylphosphonates as bridging units on resorcinarenes leads to the formation of three major isomers, namely iioo, ioio and iooo. No traces of the iiii and iiio were observed. Minor amounts of the oooo isomers are present when the R^1 group is H or CH_3 .

^{13}C NMR relaxation times

In the absence of a crystal structure of any of the possible isomers, useful information with regard to the configuration of these stereoisomers in solution has been obtained by comparison of the ^{13}C NMR relaxation parameters of **8c** (iioo isomer): in fact, the R^2 groups pointed inwards experience a reduced mobility due to the limited space in the cavity.

The ^1H NMR spectrum of **8c** at room temperature presents, in the aromatic region, seven groups of signals, whose chemical shifts, intensity and multiplicity are reported in Table 4.

The first two signals at 8.22 and 7.66 ppm do not exhibit any low frequency shift; therefore, they can be tentatively assigned to the *ortho* and *para* protons on the aromatic rings pointed outward.

To further support this hypothesis, we have followed the same approach used for the assignment of the configuration in the case of phosphate bridged cavitands.² It consists of: (i) a complete comprehension of the ^{13}C NMR spectra, at least for all protonated carbons; (ii) the determination of the ^{13}C T_1 relaxation times of the carbons on the aryl substituents bound to the phosphorous atom; (iii) a correlation of the carbon signals on the outward and inward aromatic rings and the corresponding ^1H NMR signals by means of a hetero-correlated 2D NMR experiment (HETCOR).

Note that the direct relaxation correlating $1/T_1$ (^{13}C) and the correlation times is valid only if the extreme narrowing condition is guaranteed. But we already verified on very similar compounds² that, despite the high molecular weights, correlation times are always sufficiently short. We can reasonably suppose that these conclusions can be extrapolated to all cavitands as well.

The ^{13}C NMR chemical shifts of all signals are reported

Table 5 ^{13}C NMR chemical shifts and relaxation times T_1 for isomer **8c** in CDCl_3 at 25 °C

Carbon	δ_{C}	δ_{C}	T_1/s
<i>para</i>	133.79–133.75		0.40
<i>ortho out</i>	132.03	131.89	1.71/1.70
<i>ortho in</i>	131.58	131.45	0.36/0.34
<i>meta out</i>	128.85	128.63	0.84/0.83
<i>meta in</i>	128.77	128.55	0.38/0.36
Ar(a)	120.88		0.18
Ar(b)	120.56	120.21	0.18/0.20
CH	37.90	37.80	0.20/0.21
CH ₂ (a)	31.57	31.13	0.18/0.13
CH ₂ (b)	27.88	27.67	0.27/0.26
CH ₂ (c)	29.38	29.33	0.52/0.50
CH ₂ (d)	31.84	31.78	0.92/0.94
CH ₂ (e)	22.61	22.61	1.56
CH ₃	14.07	14.01	2.40/2.41

in Table 5. Also in Table 5, the (^{13}C) T_1 relaxation times are reported. The carbon signals on the aryl groups of the **iiio** isomer directed inwards or outwards have different chemical shifts. Moreover, due to the low symmetry of the structure (C_1), the *ortho* and *meta* carbon signals on the same aryl group are all split into doublets. As can be seen clearly in Table 5, the doublet signals are sharply separated in two groups. The signals of the first group can be assigned to the *ortho* and *meta* carbons on the outward aromatic rings, because they are characterized by larger T_1 values, corresponding to shorter correlation times and therefore to a higher mobility (whose main components are overall tumbling plus internal rotation); the signals of the second group are characterized by smaller T_1 values, which are easily attributed to a more hindered internal rotation, and therefore assigned to the *ortho* and *meta* carbons of the inward aromatic rings. For the *para* carbons, the assignment is more complicated because they all overlap giving one broad signal at 133.7 ppm. The value of T_1 thus measured is actually a composite T_1 , arising from two different kinds of carbons. A proper analysis could only be done by separating the two contributions through deconvolution. The signals at about 120 ppm are assigned to the aromatic carbons on the resorcinol moiety and are all characterized by smaller T_1 values. In this case the mobility is only given by the overall tumbling, without any contribution from internal rotation. The aliphatic chains are characterized by relaxation times that increase with the distance from the resorcinol moiety, corresponding to an increase in internal mobility. The increase in relaxation times is accompanied by a decrease in the distance between the two signals relative to each carbon, because the differences in the spatial arrangement induced by the symmetry of the structure become less pronounced. On the basis of these observations a complete assignment of the signals of the aliphatic chain has been achieved (Table 5).

Then the carbon signals on the outward and inward aromatic rings were correlated to the corresponding ^1H NMR signals by means of a hetero-correlated 2D NMR experiment (HETCOR). The proton signal at 8.22 ppm, which is coupled to the ^{13}C NMR signal at 132 ppm, is assigned to the *ortho* carbons on the outward aromatic rings, thus confirming what was previously supposed. The proton signal at 7.54 ppm is coupled to the *meta* carbons at 128.8 and 128.6 ppm, which are always on the outward aromatic rings. The proton signals at 7.13 and 7.06 ppm, effectively shifted to low frequencies, are coupled to the carbon signals at 131.6–131.4 and 128.8–128.5 ppm respectively, and are assigned to the *ortho* and *meta* carbons on the inward aromatic rings. Both the *para* proton signals at 7.66 and 7.41 ppm converge towards the signal at 133.7 ppm for all *para* carbons. These results demonstrate that only the ^1H NMR signals experience the low frequency shift induced by the cavity, while the corresponding carbon signals follow the common sequence $\delta(\textit{para}) > \delta(\textit{ortho}) > \delta(\textit{meta})$. The

carbon atoms in the same position on the inward or outward aromatic rings do not show any significant difference in chemical shifts.

Conclusions

In this work we have explored the stereochemical course of the bridging reaction of resorcinarenes to form phosphonate cavitands. The configuration of all isomers has been assigned on the basis of their ^1H and ^{31}P NMR spectra and ^{13}C relaxation times. These latter measurements unambiguously proved that the upfield shift experienced by the protons of the phenyl substituents on phosphorus are diagnostic of intramolecular cavity inclusion. Therefore they can be used for configurational assignment in phosphonate cavitands. Furthermore, the presence of a ^1H – ^{31}P coupling constant in the methine resonance of the dioxaphosphocino rings is diagnostic of the inward orientation of the P=O group.

Contrary to expectations, the molecules tend to fill their cavities with phenyl substituents, leaving the P=O groups outside. This tendency is already evident in mono- and di-substituted phosphonate bridged cavitands **10a,b** and **12a,b** where the **o** and **io** isomers are dominant. The presence of more than one phenyl group pointing directly towards the centre of the cavity introduces severe steric crowding into the molecule. It can be overcome assuming that other stabilising interactions, namely intramolecular edge-to-face aromatic interactions between the electron rich resorcinarene cavity and the acidic aromatic hydrogens *ortho* to the phosphorus atoms, play an important role.⁹ This assumption is supported by the remarkable upfield shift observed for all the *ortho* hydrogens of the phenyl rings pointing inward, caused by the ring current shielding from the aromatic cavity.¹⁰ CPK model examination clearly shows that the phenyl groups pointing inward must adopt a tilted T-conformation, where one of the *ortho* protons is located at interacting distances (<3 Å) with two adjacent aromatic rings of the resorcinarene skeleton.

The overall effect favours the formation of **iooo**, **ioio** and **iiio** isomers, which represent the best compromise between steric hindrance and edge-to-face aromatic interactions. The **iiiii** isomer reported in ref. 3 becomes the dominant product of the bridging reaction only if a specific template molecule is added to the solution.¹¹

Experimental

General methods

ACS grade reagents were used without further purification. Dry acetone was distilled from phosphorus pentoxide and stored over 3 Å molecular sieves. Phenylphosphonic dichloride was purchased from Janssen Chimica. Analytical TLC was performed on Merck silica gel 60 F₂₅₄ precoated plates. Preparative TLC employed glass-backed silica gel plates with a concentration zone (Merck 60 F₂₅₄). Column chromatography was performed using silica gel (ICN, 63–200 mesh ASTM). Analyses of isomer distribution were carried out with HPLC apparatus using UV-detection at 254 nm on a 250 × 4 mm LiChrospher Si 60 column. ^1H NMR spectra were recorded at 400 and 300 MHz on Bruker AMX-400 and AC-300 spectrometers. ^{31}P NMR spectra were recorded at 161.9 and 81.0 MHz on Bruker AMX-400 and XP-200 spectrometers. Chemical shifts are given in ppm ($\delta_{\text{TMS}} = 0$) using as internal reference the residual solvent resonances of deuteriated solvents (7.25 ppm for chloroform; J values are given in Hz). ^{31}P NMR chemical shifts were measured relative to H_3PO_4 (85%) as the internal standard. IR spectra were recorded with a Nicolet SPC FTIR instrument. Mass spectra were recorded on a Finnigan-MAT SSQ 710 mass spectrometer using the DCI technique. Elemental analyses were performed by the services of Leipzig and Parma Universities.

Resorcinarenes **1–4**, **9** and **11** were obtained following published procedures.^{5,6}

1,21,23,25-Tetramethyl-5,9,13,17-tetroxo-5,9,13,17-tetra-phenyl-2,20:3,19-dimetheno-1,21,23,25-tetrahydro[1,3,2λ⁵]-dioxaphosphocino[4''',5''':4''',5''']benzo[1''',2''':7''',8'''] [1,3,2λ⁵]-dioxaphosphocino[4''',5''':4''',5''']benzo[1''',2''':7''',8'''] [1,3,2λ⁵]-dioxaphosphocino[5',4':4,5]benzo[1,2-d][1,3,2λ⁵]-dioxaphosphocine **5**

To a stirred solution of resorcinarene **1** (1.57 g, 2.9 mmol) in 150 ml dry acetone triethylamine (4.03 ml, 29 mmol) was added with a syringe at once. A solution of phenylphosphonic dichloride (2.81 g, 14.5 mmol) in 50 ml dry acetone was then added dropwise over 2 h. The reaction mixture was stirred for 6 h at room temperature. The solid triethylammonium chloride formed was filtered off and washed with 50 ml acetone. The solvent was removed *in vacuo* and the resulting viscous residue dried at the vacuum pump. Purification by column chromatography on silica gel with 6:1 CH₂Cl₂–acetone as eluent afforded four isomeric products in 50% overall yield: **5b** (isomer **iooo**), white solid (930 mg, 31%), mp >360 °C, *R_f* 0.43; **5a** (isomer **oooo**), white solid (90 mg, 3%), mp >360 °C, *R_f* 0.32; **5d** (isomer **ioio**), white solid (180 mg, 6%), mp >360 °C, *R_f* 0.27; **5c** (isomer **iiio**), white solid (300 mg, 10%), mp >360 °C, *R_f* 0.17.

5a. ν_{\max} (KBr pellet)/cm⁻¹ 1277 (P=O, br); δ_{H} (400 MHz; CDCl₃) 1.92 (12H, d, *J* 6.8), 5.24 (4H, q, *J* 6.8), 6.37 (4H, t, *J*_{HP} 1.1), 7.20 (8H, m, ArH_o out), 7.27 (4H, s), 7.28 (8H, m, ArH_m out), 7.38 (4H, m, ArH_p out); δ_{P} (81.0 MHz; CDCl₃) 9.03 (4P, t, *J* 14); *m/z* (DCI) 1033 (M⁻, 100%); (Found: C, 64.82; H, 4.31. C₅₆H₄₄O₁₂P₄ requires C, 65.12; H, 4.29%).

5b. ν_{\max} (KBr pellet)/cm⁻¹ 1277 (P=O, br); δ_{H} (400 MHz; CDCl₃) 1.86 (3H, d, *J* 7.3), 1.91 (3H, d, *J* 7.0), 1.94 (6H, d, *J* 7.0), 5.02 (1H, dq, *J*₁ 7.3, *J*_{HP} 2.0), 5.18 (1H, q, *J* 7.0), 5.29 (2H, q, *J* 7.0), 6.38 (2H, s), 6.68 (2H, t, *J*_{HP} 1.5), 7.22–7.34 (9H, m, ArH_p out, ArH_m out), 7.31 (2H, s), 7.32 (2H, s), 7.51 (8H, m, ArH_o out, ArH_m in), 7.66 (1H, m, ArH_p in), 8.00 (2H, ddd, *J*_{HP} 14.2, *J*₂ 7.0, *J*₃ 1.3, ArH_o in); δ_{P} (81.0 MHz; CDCl₃) 9.34 (2P, t, *J* 14), 9.64 (1P, t, *J* 14), 10.94 (1P, t, *J* 14); *m/z* (DCI) 1033 (M⁻, 100%); (Found: C, 65.03; H, 4.40. C₅₆H₄₄O₁₂P₄ requires C, 65.12; H, 4.29%).

5c. ν_{\max} (KBr pellet)/cm⁻¹ 1276 (P=O, br); δ_{H} (400 MHz; CDCl₃) 1.92 (6H, d, *J* 7.0), 1.94 (6H, d, *J* 7.2), 5.04 (2H, dq, *J*₁ 7.0, *J*_{HP} 2.1), 5.23 (2H, q, *J* 7.2), 6.28 (1H, t, *J*_{HP} 1.2), 6.56 (2H, t, *J*_{HP} 1.2), 6.93 (2H, m, ArH_p out), 6.97 (1H, s), 7.03 (4H, m, ArH_m out), 7.11 (1H, t, *J*_{HP} 1.2), 7.34–7.56 (11H, m), 7.65 (2H, m, ArH_p in), 8.04 (4H, dd, *J*_{HP} 14.2, *J*₂ 7.5, ArH_o in); δ_{P} (81.0 MHz; CDCl₃) 7.62 (2P, t, *J* 14), 10.34 (2P, t, *J* 14); *m/z* (DCI) 1033 (M⁻, 100%); (Found: C, 65.40; H, 4.51. C₅₆H₄₄O₁₂P₄ requires C, 65.12; H, 4.29%).

5d. ν_{\max} (KBr pellet)/cm⁻¹ 1276 (P=O, br); δ_{H} (400 MHz; CDCl₃) 1.88 (6H, d, *J* 6.9), 1.94 (6H, d, *J* 7.3), 5.05 (2H, dq, *J*₁ 6.9, *J*_{HP} 2.2), 5.48 (2H, q, *J* 7.3), 6.73 (4H, t, *J*_{HP} 0.8), 7.34 (4H, s), 7.42 (4H, m, ArH_m out), 7.53 (6H, m, ArH_p out, ArH_m in), 7.63 (2H, m, ArH_p in), 7.71 (4H, dd, *J*_{HP} 14.6, *J*₂ 2.2, ArH_o out), 8.02 (4H, dd, *J*_{HP} 14.2, *J*₂ 7.2, ArH_o in); δ_{P} (81.0 MHz; CDCl₃) 9.02 (2P, t, *J* 14), 9.89 (2P, t, *J* 14); *m/z* (DCI) 1033 (M⁻, 100%); (Found: C, 64.97; H, 4.27. C₅₆H₄₄O₁₂P₄ requires C, 65.12; H, 4.29%).

1,7,11,15,21,23,25-Octamethyl-5,9,13,17-tetroxo-5,9,13,17-tetra-phenyl-2,20:3,19-dimetheno-1,21,23,25-tetrahydro[1,3,2λ⁵]-dioxaphosphocino[4''',5''':4''',5''']benzo[1''',2''':7''',8'''] [1,3,2λ⁵]-dioxaphosphocino[4''',5''':4''',5''']benzo[1''',2''':7''',8'''] [1,3,2λ⁵]-dioxaphosphocino[5',4':4,5]benzo[1,2-d][1,3,2λ⁵]-dioxaphosphocine **6**

Compounds **6a–d** were obtained following the above procedure, using as starting material resorcinarene **2** (3 mmol). Purification of the crude material by column chromatography on silica gel with 6:1 CH₂Cl₂–acetone as eluent afforded four isomeric

products in 30% overall yield: **6b** (isomer **iooo**), white solid (396 mg, 15%), *R_f* 0.62; **6a** (isomer **oooo**), white solid (40 mg, 2%), mp >360 °C, *R_f* 0.51; **6c** (isomer **iiio**), white solid (223 mg, 8%), mp >360 °C, *R_f* 0.34. Isomers **6d** (isomer **ioio**) could not be obtained in pure form, but only as a mixture with **6b**. HPLC chromatography of the **6b–6d** mixture (123 mg) indicates a 1:1 ratio between the two isomers.

6a. ν_{\max} (KBr pellet)/cm⁻¹ 1260 (P=O, br); δ_{H} (400 MHz; CDCl₃) 1.34 (12H, s), 1.94 (12H, d, *J* 7.2), 5.27 (4H, q, *J* 7.2), 6.80–7.02 (16H, m), 7.33 (4H, m); δ_{P} (81.0 MHz; CDCl₃) 5.87 (4P, t, *J* 14); *m/z* (DCI) 1089 (M⁻, 100%); (Found: C, 66.57; H, 4.57. C₆₀H₅₂O₁₂P₄ requires C, 66.18; H, 4.81%).

6b. ν_{\max} (KBr pellet)/cm⁻¹ 1260 (P=O, br); δ_{H} (400 MHz; CDCl₃) 1.31 (6H, s), 1.76 (6H, s), 1.86 (3H, d, *J* 7.3), 1.88 (3H, d, *J* 7.1), 1.94 (6H, d, *J* 7.0), 5.0 (1H, dq, *J*₁ 7.3, *J*_{HP} 2.3), 5.13 (1H, q, *J* 7.1), 5.27 (2H, q, *J* 7.0), 6.75 (2H, dd, *J*_{HP} 13.7, *J*₂ 7.2, ArH_o out), 6.95 (2H, m, ArH_m out), 7.10–7.20 (9H, m), 7.32 (2H, s), 7.35 (2H, s), 7.40–7.55 (4H, m, ArH_p out, ArH_m in), 7.63 (1H, m, ArH_p in), 7.96 (2H, ddd, *J*_{HP} 14.1, *J*₂ 7.0, *J*₃ 1.3, ArH_o in); δ_{P} (81.0 MHz; CDCl₃) 5.34 (2P, t, *J* 14), 7.00 (1P, t, *J* 14), 9.94 (1P, t, *J* 14); *m/z* (DCI) 1089 (M⁻, 100%); (Found: C, 66.03; H, 5.16. C₆₀H₅₂O₁₂P₄ requires C, 66.18; H, 4.81%).

6c. ν_{\max} (KBr pellet)/cm⁻¹ 1255 (P=O, br); δ_{H} (400 MHz; CDCl₃) 1.26 (3H, s), 1.59 (6H, s), 1.91 (6H, d, *J* 7.3), 1.94 (6H, d, *J* 7.1), 2.27 (3H, s), 5.02 (2H, dq, *J*₁ 7.3, *J*_{HP} 1.8), 5.15 (2H, q, *J* 7.1), 6.75 (4H, dd, *J*_{HP} 13.7, *J*₂ 7.7, ArH_o out (4H, m, ArH_m out), 7.34 (1H, s), 7.39 (2H, m, ArH_p out), 7.41 (3H, s), 7.55 (4H, m, ArH_m in), 7.65 (2H, m, ArH_p in), 8.03 (4H, ddd, *J*_{HP} 14.2, *J*₂ 7.1, *J*₃ 1.4, ArH_o in); δ_{P} (81.0 MHz; CDCl₃) 3.61 (2P, t, *J* 14), 9.11 (2P, t, *J* 14); *m/z* (DCI) 1089 (M⁻, 100%); (Found: C, 65.96; H, 5.15. C₆₀H₅₂O₁₂P₄ requires C, 66.18; H, 4.81%).

7,11,15,28-Tetrabromo-1,21,23,25-tetramethyl-5,9,13,17-tetroxo-5,9,13,17-tetra-phenyl-2,20:3,19-dimetheno-1,21,23,25-tetrahydro[1,3,2λ⁵]-dioxaphosphocino[4''',5''':4''',5''']benzo[1''',2''':7''',8'''] [1,3,2λ⁵]-dioxaphosphocino[4''',5''':4''',5''']benzo[1''',2''':7''',8'''] [1,3,2λ⁵]-dioxaphosphocino[5',4':4,5]benzo[1,2-d][1,3,2λ⁵]-dioxaphosphocine **7**

To a stirred solution of resorcinarene **3** (0.70 g, 0.81 mmol) in 80 ml dry THF, triethylamine (1.13 ml, 8.1 mmol) was added with a syringe at once. A solution of phenylphosphonic dichloride (0.80 g, 4.1 mmol) in 30 ml dry THF was then added dropwise over 2 h. The reaction mixture was stirred for 6 h at room temperature. The solid triethylammonium chloride formed was filtered off and washed with 30 ml THF. The solvent was removed *in vacuo* and the resulting viscous residue dried at the vacuum pump. Purification by column chromatography on silica gel with 86:14 CH₂Cl₂–acetone as eluent afforded three isomeric products in 35% overall yield: **7c** (isomer **iiio**), white solid (77 mg, 7%), mp >360 °C, *R_f* 0.78; **7d** (isomer **ioio**), white solid (306 mg, 28%), mp >360 °C, *R_f* 0.60. The third isomer **7b** (**iooo**) is present only in traces.

7c. ν_{\max} (KBr pellet)/cm⁻¹ 1264 (P=O); δ_{H} (300 MHz; CDCl₃) 1.86 (6H, d, *J* 7.3), 1.98 (6H, d, *J* 7.3), 5.02 (2H, dq, *J* 7.3, *J*_{HP} 1.5), 5.54 (2H, q, *J* 6.8), 7.27–7.34 (4H, m, ArH_o out), 7.42 (3H, s), 7.46–7.56 (11H, m), 7.61 (2H, m, ArH_p in), 8.15 (4H, ddd, *J*_{HP} 14.4, *J*₂ 7.9, *J*₃ 1.4, ArH_o in); δ_{P} (81.0 MHz; CDCl₃) 5.72 (2P, t, *J* 14), 8.96 (2P, t, *J* 14); *m/z* (DCI) 1348 (M⁺, 100%); (Found: C, 49.78; H, 3.03. C₅₆H₄₀Br₄O₁₂P₄ requires C, 49.88; H, 2.99%).

7d. ν_{\max} (KBr pellet)/cm⁻¹ 1264 (P=O); δ_{H} (300 MHz; CDCl₃) 1.87 (6H, d, *J* 7.3), 1.96 (6H, d, *J* 7.3), 5.05 (2H, dq, *J*₁ 7.3, *J*_{HP} 1.8), 5.48 (2H, q, *J* 6.8), 6.67 (4H, s), 7.10–7.17 (4H, m, ArH_o out), 7.29–7.37 (4H, m, ArH_m out), 7.40–7.48 (2H, m, ArH_p out), 7.51–7.58 (4H, m, ArH_m in), 7.64–7.67 (2H, m, ArH_p in), 8.23 (4H, m, ddd, *J*_{HP} 14.4, *J*₂ 7.9, *J*₃ 1.4, ArH_o in); δ_{P} (81.0 MHz; CDCl₃) 6.65 (2P, t, *J* 14), 9.25 (2P, t, *J* 14); *m/z* (DCI) 1348 (M⁺, 100%); (Found: C, 49.75; H, 3.02. C₅₆H₄₀Br₄O₁₂P₄ requires C, 49.88; H, 2.99%).

7,11,15,28-Tetrabromo-1,21,23,25-tetrahexyl-5,9,13,17-tetroxo-5,9,13,17-tetraphenyl-2,20:3,19-dimetheno-1,21,23,25-tetrahydro[1,3,2λ⁵]dioxaphosphocino[4''',5''':4''',5''']benzo[1''',2''':7''',8'''][1,3,2λ⁵]dioxaphosphocino[4''',5''':4''',5''']benzo[1'',2'':7'',8''][1,3,2λ⁵]dioxaphosphocino[5',4':4,5]benzo[1,2-d][1,3,2λ⁵]dioxaphosphocine **8**

Compounds **8b–d** were obtained following the above procedure, using as starting material resorcinarene **4** (1.8 mg, 1.6 mmol). Purification of the crude product by column chromatography on silica gel with 88:12 CH₂Cl₂–acetone as eluent afforded three isomeric products in 44% overall yield: **8b** (isomer **iooo**), white solid (260 mg, 10%), mp 210 °C (decomp.), *R_f* 0.85; **8d** (isomer **ioio**), white solid (200 mg, 8%), mp 220 °C (decomp.), *R_f* 0.80; **8c** (isomer **ioo**), white solid (680 mg, 26%), mp 215 °C (decomp.), *R_f* 0.58.

8b. ν_{\max} (KBr pellet)/cm⁻¹ 1265 (P=O); δ_{H} (300 MHz; CDCl₃) 0.84–0.97 (12H, m), 1.29–1.50 (32H, m), 2.25 (2H, m), 2.36 (6H, m), 4.75 (1H, dt, *J*₁ 15, *J*_{HP} 1.6), 5.13 (1H, t, *J* 15), 5.27 (2H, t, *J* 15), 7.03–7.11 (6H, m, ArH_o out), 7.15–7.23 (6H, m, ArH_m out), 7.24 (2H, s), 7.27 (2H, s), 7.35–7.43 (3H, m, ArH_p out), 7.46–7.55 (2H, m, ArH_m in), 7.64 (2H, t, *J* 14.7, ArH_p in), 8.19 (2H, ddd, *J*_{HP} 14.5, *J*₂ 7.8, *J*₃ 1.3, ArH_o in); δ_{P} (81.0 MHz; CDCl₃) 8.68 (2P, t, *J* 14), 9.87 (1P, t, *J* 14), 10.33 (1P, t, *J* 14); *m/z* (DCI) 1629 (M⁺, 100%) (Found: C, 56.09; H, 4.97. C₇₆H₈₀Br₄O₁₂P₄ requires C, 56.04; H, 4.95%).

8c. ν_{\max} (KBr pellet)/cm⁻¹ 1265 (P=O); δ_{H} (300 MHz; CDCl₃) 0.89 (6H, t, *J* 13.4), 0.91 (6H, t, *J* 13.4), 1.27–1.47 (32H, m), 2.31 (4H, m), 2.38 (4H, m), 4.79 (2H, t, *J* 15.1), 5.20 (2H, t, *J* 15.1), 7.03–7.10 (4H, m, ArH_o out), 7.11–7.16 (4H, m, ArH_m out), 7.31 (3H, s), 7.36 (1H, s), 7.41 (2H, t, *J* 13.2, ArH_p out), 7.50–7.57 (4H, m, ArH_m in), 7.66 (2H, t, *J* 12.4, ArH_p in), 8.22 (4H, ddd, *J*_{HP} 14.5, *J*₂ 7.8, *J*₃ 1.3, ArH_o in); δ_{C} (75 MHz; CDCl₃) 14.01, 14.07 (CH₃), 22.61 [CH₃(CH₂)₄CH₂], 27.67, 27.88 [CH₃CH₂(CH₂)₄], 29.33, 29.38 [CH₃(CH₂)₂CH₂(CH₂)₂], 31.13, 31.57 [CH₃CH₂(CH₂)₄], 31.78, 31.84 [CH₃(CH₂)₃CH₂CH₂], 37.80, 37.90 (CH) 120.21, 120.56, 120.88 (Ar), 128.55, 128.77 (Ar_m out), 128.63, 128.85 (Ar_m in), 131.45, 131.58 (Ar_o out), 131.89, 132.03 (Ar_o in), 133.75–133.79 (Ar_p in, Ar_p out); δ_{P} (81.0 MHz; CDCl₃) 5.05 (2P, t, *J* 14), 9.30 (2P, t, *J* 14); *m/z* (DCI) 1629 M⁺, 100%) (Found: C, 56.01; H, 4.92. C₇₆H₈₀Br₄O₁₂P₄ requires C, 56.04; H, 4.95%).

8d. ν_{\max} (KBr pellet)/cm⁻¹ 1265 (P=O); δ_{H} (300 MHz; CDCl₃) 0.88 (6H, t, *J* 9.7), 0.92 (6H, t, *J* 9.7), 1.26–1.50 (32H, m), 2.28 (4H, m), 2.41 (4H, m), 4.72 (2H, dt, *J*₁ 15.3, *J*_{HP} 1.6), 5.26 (2H, t, *J* 15.3), 7.21–7.28 (4H, m, ArH_o out), 7.30–7.35 (4H, m, ArH_m out), 7.33 (4H, s), 7.45 (2H, m, ArH_p out), 7.45–7.51 (4H, m, ArH_m in), 7.60 (2H, t, *J* 15, ArH_p in), 8.11 (4H, ddd, *J*_{HP} 14.5, *J*₂ 7.8, *J*₃ 1.3, ArH_o in); δ_{P} (81.0 MHz; CDCl₃) 4.83 (2P, t, *J* 14), 9.39 (2P, t, *J* 14); *m/z* (DCI) 1629 (M⁺, 100%) (Found: C, 56.08; H, 4.90. C₇₆H₈₀Br₄O₁₂P₄ requires C, 56.04; H, 4.95%).

7,11,15,28-Tetrabromo-1,21,23,25-tetramethyl-5-oxo-5-phenyl-2,20:3,19-dimetheno-9,13,17,21,23,25-hexahydro-1H-[1,3]-dioxacino[4''',5''':4''',5''']benzo[1''',2''':7''',8'''][1,3]dioxacino[4''',5''':4''',5''']benzo[1'',2'':7'',8''][1,3]dioxacino[5',4':4,5]benzo[1,2-d][1,3,2λ⁵]dioxaphosphocine **10**

To a stirred solution of tri-bridged cavitand **9** (500 mg, 0.558 mmol) in 30 ml dry acetone, triethylamine (0.78 ml, 5.6 mmol) was added with a syringe. A solution of phenylphosphonic dichloride (544 mg, 2.79 mmol) in 10 ml dry acetone was then added dropwise over 2 h. The reaction mixture was stirred for one day at room temperature. The solid triethylammonium chloride formed was filtered off. The solvent of the remaining solution was removed *in vacuo* and the resulting solid was dried at the vacuum pump. Purification by column chromatography on silica gel with 3:2 hexane:ethyl acetate as eluent afforded two isomeric products in 44% overall yield: **10b** (isomer **i**), white solid (88 mg, 15%), mp >300 °C (decomp.), *R_f* 0.47; **10a** (isomer **o**), white solid (165 mg, 29%), mp >360 °C (decomp.), *R_f* 0.32.

10a. ν_{\max} (KBr pellet)/cm⁻¹ 1267 (P=O); δ_{H} (300 MHz; CDCl₃) 1.76 (3H, d, *J* 7.5), 1.79 (6H, d, *J* 7.4), 1.87 (3H, d, *J* 7.2), 4.07 (2H, d, *J* 7.3), 4.33 (1H, d, *J* 7.4), 5.09 (1H, q, *J* 7.5), 5.12 (2H, q, *J* 7.4), 5.37 (1H, q, *J* 7.2), 5.83 (2H, d, *J* 7.3), 6.02 (1H, d, *J* 7.3), 6.82 (2H, m, ArH_o out), 7.17 (2H, m, ArH_m out), 7.21 (2H, s), 7.28 (2H, s), 7.37 (1H, m, ArH_p out); δ_{P} (81.0 MHz; CDCl₃) 7.56 (1P, t, *J* 14); *m/z* (DCI) 1018 (M⁺, 100%) (Found: C, 48.67; H, 3.44. C₄₁H₃₁Br₄O₉P requires C, 48.36; H, 3.07%).

10b. ν_{\max} (KBr pellet)/cm⁻¹ 1277 (P=O); δ_{H} (300 MHz; CDCl₃) 1.73 (3H, d, *J* 7.4), 1.79 (9H, d, *J* 7.4), 4.58 (1H, d, *J* 7.3), 4.64 (2H, d, *J* 7.3), 4.95 (1H, dq, *J*₁ 7.4, *J*_{HP} 2.4), 5.05 (1H, q, *J* 7.4), 5.13 (2H, q, *J* 7.4), 5.90 (2H, d, *J* 7.3), 5.99 (1H, d, *J* 7.3), 7.18 (2H, s), 7.22 (2H, s), 7.59 (2H, m, ArH_m in), 7.68 (1H, m, ArH_p in), 8.29 (2H, ddd, *J*_{HP} 14.5, *J*₂ 8.0, *J*₃ 1.5, ArH_o in); δ_{P} (81.0 MHz; CDCl₃) 8.84 (1P, t, *J* 14); *m/z* (DCI) 1018 (M⁺, 100%) (Found: C, 48.51; H, 3.32. C₄₁H₃₁Br₄O₉P requires C, 48.36; H, 3.07%).

7,11,15,28-Tetrabromo-1,21,23,25-tetramethyl-5,13-dioxo-5,13-diphenyl-2,20:3,19-dimetheno-1,9,17,21,23,25-hexahydro-[1,3]-dioxacino[4''',5''':4''',5''']benzo[1''',2''':7''',8'''][1,3,2λ⁵]dioxaphosphocino[4''',5''':4''',5''']benzo[1'',2'':7'',8''][1,3]dioxacino[5',4':4,5]benzo[1,2-d][1,3,2λ⁵]dioxaphosphocine **12**

To a stirred solution of di-bridged cavitand **11** (185 mg, 0.209 mmol) in 20 ml dry acetone, triethylamine (0.58 ml, 4.2 mmol) was added with a syringe. A solution of phenylphosphonic dichloride (440 mg, 2.26 mmol) in 5 ml dry acetone was then added dropwise over 2 h. The reaction mixture was stirred for one day at room temperature. The solid triethylammonium chloride formed was filtered off. The solvent was removed *in vacuo* from the filtrate and the resulting solid was dried at the vacuum pump. Purification by column chromatography on silica gel with 19:1 CH₂Cl₂–hexane as eluent afforded two isomeric products in 30% overall yield with compound **12b** (isomer **io**) as major component, white solid, mp >270 °C (decomp.), *R_f* 0.48. Compound **12a** (isomer **oo**) could only be isolated in a 1:4 mixture with **12b** (checked by analytical HPLC and confirmed by ¹H NMR integration).

12a. δ_{H} (400 MHz; CDCl₃) 1.79 (6H, d), 1.80 (6H, d), 4.80 (2H, d, *J* 7.3), 5.02 (2H, q), 5.13 (2H, q), 5.91 (2H, d, *J* 7.3), 7.32 (4H, s), 7.60 (6H, m), 8.28 (4H, m); δ_{P} (81.0 MHz; CDCl₃) 7.94 (2P, t, *J* 14).

12b. ν_{\max} (KBr pellet)/cm⁻¹ 1278 and 1265 (P=O); δ_{H} (400 MHz; CDCl₃) 1.82 (3H, d, *J* 7.4), 1.85 (6H, d, *J* 7.5), 1.89 (3H, d, *J* 7.4), 4.06 (2H, d, *J* 7.4), 5.14 (1H, dq, *J*₁ 7.4, *J*_{HP} 2.1), 5.14 (2H, q, *J* 7.5), 5.27 (1H, q, *J* 7.4), 5.80 (2H, d, *J* 7.4), 6.81 (2H, m, ArH_m out), 6.88 (2H, m, ArH_o out), 7.34 (2H, s), 7.35 (2H, s), 7.39 (1H, m, ArH_p out), 7.60 (2H, m, ArH_m in), 7.70 (1H, m, ArH_p in), 8.31 (2H, dd, *J*_{HP} 14.5, *J*₂ 8.0, *J*₃ 1.3, ArH_o in); δ_{P} (81.0 MHz; CDCl₃) 6.81 (1P, t, *J* 14), 9.77 (1P, t, *J* 14); *m/z* (DCI) 1128 (M⁺, 100%) (Found: C, 50.12; H, 3.19. C₄₆H₃₄Br₄O₁₀P₂ requires C, 48.97; H, 3.04%).

¹³C Relaxation times experiments

¹³C NMR spectra were recorded in BB proton decoupling, with scan width = 11 900 Hz, relaxation delay = 2 s and pulse width = 70°. Chemical shifts are referred to the residual signal of CDCl₃ at 77.0 ppm. The *T*₁(¹³C) measurements were performed in NMR tubes sealed under vacuum. The standard Inversion-Recovery method was used, with proton decoupling during acquisition. The parameters for the *T*₁ measurements are: six τ values, in the range 0.1–10 s, a recovery delay of 10 s and 2560 scans for each τ value. The HETCOR experiment was performed with the standard pulse sequence and the following acquisition parameters: spectral width = 11 900 Hz in F2, 3400 Hz in F1; digital resolution = 11.6 Hz/pt in F2, 3.3 Hz/pt in F1; relaxation delay = 1 s; 256 increments with 768 scans for each increment.

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¹H, ¹³C and HETCOR NMR spectra of compound **8c** are available as supplementary material (SUPPL. No. 57326, 5 pp.). For details of the Supplementary Publications Scheme see 'Instructions for Authors', *J. Chem. Soc., Perkin Trans. 2*, available via the RSC Web page (<http://chemistry.rsc.org/authors>).

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