

# An efficient preparation of macrocycles containing two tetra-coordinate phosphorus atoms

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## Abstract

The Staudinger reaction between bis(azides) and bis(phosphines) under mild conditions provides macrocyclic bis(iminophosphoranes) (at least 12-membered rings) in excellent to moderate yield. The method also allows the incorporation of a heteroatom into the chain connecting the two aromatic or heteroaromatic rings.

*Keywords:* Bis(azides); Bis(phosphines); Staudinger reaction; Macrocyclic bis(iminophosphoranes)

## 1. Introduction

Since the discovery by Pedersen [1] of the complex-forming properties of macrocyclic polyethers, a plethora of studies, not only on the use of the complex-forming phenomenon, but also on the synthesis of new macrocyclic systems, has appeared. In this context, improvements which increase the efficiency or enlarge the applicability of the macrocyclic ligands by introducing into the ring the iminophosphorane moiety, which possesses a high complex-forming capacity with a wide variety of metal compounds [2] and metal carbonyls [3], is important in this respect.

Although the synthesis and thermodynamic and kinetic data for cation-macrocycle interactions of phosphorus-containing macrocycles possessing an intracyclic C–P–N grouping have been previously reported [4–6], we wish to report now the preparation of macrocycles containing two tetra-coordinate phosphorus atoms (at least 12-membered rings) bearing two iminophosphorane moieties (macrocyclic bis(iminophosphoranes)). Our approach is based on the Staudinger reaction of bis(azides) with bis(phosphines) of general structure  $R_2P-Y-PR_2$ , which has been recently used by Majoral and coworkers [7] for the preparation of phosphorus-containing cryptands.

## 2. Results and discussion

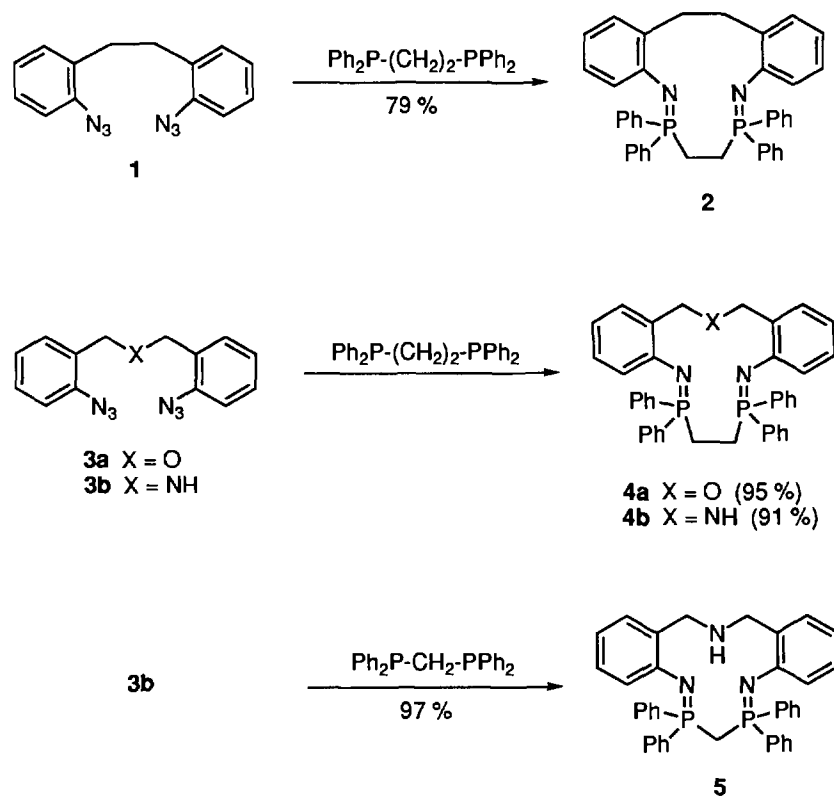
The bis(azide) **1** [8] reacts with 1,2-bis(diphenylphosphino)ethane in dichloromethane at room temperature to give the macrocyclic bis(iminophosphorane) **2** in excellent yield (79%).

The incorporation of a heteroatom into the chain connecting the two aromatic rings has also been examined. Thus, the bis(azide) **3a** [8] reacts with the same bis(phosphine) under similar reaction conditions to give the 13-membered bis(iminophosphorane) **4a** in almost quantitative yield as a crystalline solid. The related bis(azide) **3b** [9] provided the macrocyclic bis(iminophosphorane) **4b** in excellent yield (91%). A similar result is obtained when bis(diphenylphosphino)methane is used as cyclocondensation agent. Thus, the bis(azide) **3b** also reacts with bis(diphenylphosphino)methane to give the macrocyclic bis(iminophosphorane) **5**, as a crystalline solid in 97% yield (Scheme 1).

These results clearly show that the presence of an oxygen atom or an amino group into the chain connecting the two aromatic rings did not affect the behaviour observed for the bis(azide) **1**, and this fact allows us to introduce a new coordinative atom into the macrocyclic ring.

Having established that the Staudinger reaction of bis(azides) of types **1** or **3** with bis(phosphines) provided macrocyclic bis(iminophosphoranes), variations were also considered in order to evaluate the suitability

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Scheme 1.

of this reaction in producing phosphorus-containing macrocycles of varying ring size and complexity.

The condensation of 5-azido-4-formylpyrazole **6** [10] with 1,4-diaminobutane in ethanol at room temperature provided the bis(azide) **7** in moderate yield, which by treatment with 1,4-bis(diphenylphosphino)butane afforded the 20-membered macrocyclic bis(iminophosphorane) **8** as a crystalline solid in 56% yield. Likewise, starting from 5-azido-4-formyl-1,2,3-triazole **9** [10] 16-membered phosphorus-containing macrocycles **11** are obtained in moderate yields (39–41%) using the above protocol (Scheme 2).

In the  $^{13}\text{C}$  NMR spectra of these macrocyclic bis(iminophosphoranes) (**2**, **4a**, **4b**, **5**, **11a** and **11b**) the carbon atoms of the bis(phosphine) fragments as well as those from the *N*-(hetero)aryl groups which are at less than four-bond distance from the phosphorus atoms appear multisplit, as AXX' systems, due to virtual coupling [11,12] (see Section 3 or Table 1).

Although none of these compounds gave the molecular ion peak in the electron impact mass spectrum, FAB mass spectra have so far proved to be successful in confirming unambiguously all the prepared structures.

In conclusion, the Staudinger reaction between bis(azides) and bis(phosphines) provides an attractive entry to the preparation of macrocycles containing two tetra-coordinate phosphorus atoms, more specifically

two iminophosphorane moieties. The method also allows the introduction of a heteroatom into the macrocyclic framework.

### 3. Experimental

#### 3.1. General

All melting points were determined on a Kofler hot-plate melting point apparatus and are uncorrected. IR spectra were obtained on Nujol emulsions on a Nicolet Impact 400 spectrophotometer.  $^1\text{H}$  NMR,  $^{13}\text{P}$  NMR spectra were recorded at 299.95 MHz, 74.43 MHz and 121.42 MHz respectively on a Varian UNITY-300 spectrometer. Chemical shifts refer to signals of tetramethylsilane in the case of  $^1\text{H}$  and  $^{13}\text{C}$  spectra and to 85% aqueous phosphoric acid in the case of  $^{31}\text{P}$  spectra. Abbreviations of coupling patterns are as follows: s, singlet; d, doublet; t, triplet; q, quadruplet; qn, quintuplet; m, multiplet; and vm, virtual multiplet. The mass spectra were carried out on a VG-Autospec spectrometer in the FAB<sup>+</sup> mode. The starting bis(azides) **1** and **3a** [8], **3b** [9], and  $\beta$ -azidoaldehydes **6** and **9** [10] were prepared according to literature methods.

### 3.2. Preparation of imines 7 and 10

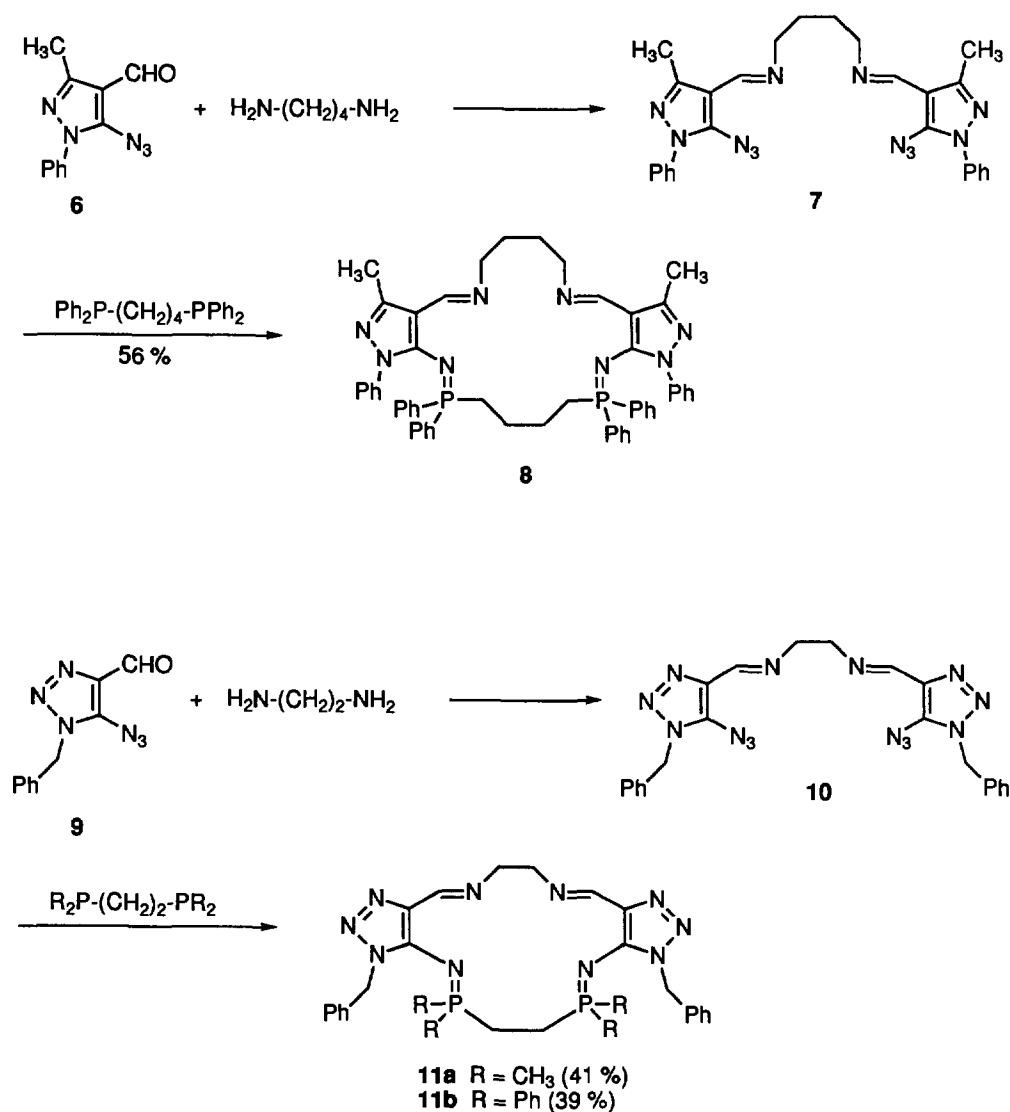
To a solution of 5-azido-4-formyl-3-methyl-1-phenyl-1*H*-pyrazole **6** or 5-azido-1-benzyl-4-formyl-1*H*-1,2,3-triazole **9** (10 mmol) in dry ethanol (25 ml) was added the appropriate diamine (5 mmol) and a catalytic amount of acetic acid. The reaction mixture was stirred for 12 h at room temperature. The crystalline precipitate was collected by filtration and recrystallized from ethanol, and was directly used in the subsequent step.

### 3.3. Preparation of bis(iminophosphoranes) 2, 4, 5, 8 and 11

To a solution of the corresponding bis(azide) (**1**, **3**, **7**, **10**) (2.5 mmol) in dry dichloromethane (100 ml) was added dropwise during 4 h, under nitrogen and at room

temperature, a solution of the bis(phosphine) (2.5 mmol) in the same solvent (100 ml). The reaction mixture was stirred at room temperature for 1 h. The solvent was removed to dryness and the resulting solid was treated with dry diethyl ether (25 ml), collected by filtration and recrystallized.

Compound **2**: yield 79%; m.p. 164–165 °C (colourless prisms from diethyl ether); IR (Nujol):  $\nu$  1590, 1452, 1338, 1114, 728  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3 + \text{CF}_3\text{COOH}$ ):  $\delta$  7.87–7.57 (20H, m), 7.36 (2H, d,  $J = 7.76$  Hz), 7.04 (2H, t,  $J = 7.28$  Hz), 6.81 (2H, t,  $J = 7.71$  Hz), 6.43 (2H, d,  $J = 7.76$  Hz), 3.52 (4H, s), 3.27 (4H, s) ppm;  $^{13}\text{C}$  NMR ( $\text{CDCl}_3 + \text{CF}_3\text{COOH}$ ):  $\delta$  136.67 (vt,  $J = 38.3$  Hz), 135.11 ( $\text{C}_p$ , s), 132.98 ( $\text{C}_o$ , vt,  $J = 10.7$  Hz), 132.60, 130.92, 130.10 ( $\text{C}_m$ , vt,  $J = 13.0$  Hz), 127.01, 125.68, 119.40 ( $\text{C}_i$ , vq,  $J = 114.3$  Hz), 34.12, 20.47 ( $\text{CH}_2\text{P}$ , vqn,  $J = 93.2$  Hz) ppm (one carbon atom resonance was not observed);  $^{31}\text{P}$  NMR ( $\text{CDCl}_3$ ):  $\delta$



Scheme 2.

Table 1  
Selected NMR data of macrocyclic bis(iminophosphoranes) <sup>a</sup>

Compound <b>4b</b>	Compound <b>5</b>	Compound <b>8</b>	Compound <b>11a</b>	Compound <b>11b</b>
<b><sup>31</sup>P NMR</b>				
12.23 (s)	5.99 (s)	9.39 (s)	25.53 (s)	12.22 (s)
<b><sup>13</sup>C NMR</b>				
150.56 (C2, vt, <sup>2</sup> J <sub>PC2</sub> + <sup>5</sup> J <sub>PCCPNC2</sub> = 3.2 Hz)	149.47 (C2, vt, <sup>2</sup> J <sub>PC2</sub> + <sup>4</sup> J <sub>PCPNC2</sub> = 3.6 Hz)	154.21 (CH = N)	156.69 (CH = N)	154.91 (CH = N)
132.16 (Cp, s)	132.10 (Cp, s)	148.77 (C5, d, <sup>2</sup> J <sub>PC5</sub> = 10.5 Hz)	143.03 (C5, vt, <sup>2</sup> J <sub>PC5</sub> + <sup>5</sup> J <sub>PCCPNC5</sub> = 4.2 Hz)	142.65 (C5, vt, <sup>2</sup> J <sub>PC5</sub> + <sup>5</sup> J <sub>PCCPNC5</sub> = 11.7 Hz)
131.59 (Co, vt, <sup>2</sup> J <sub>PCo</sub> + <sup>5</sup> J <sub>PCCPCiCo</sub> = 9.5 Hz)	131.76 (Co, vt, <sup>2</sup> J <sub>PCo</sub> + <sup>4</sup> J <sub>PCCPCiCo</sub> = 10.1 Hz)	148.73 (C3)	137.34 (C1')	137.11 (C1')
129.33 (C4)	131.12 (C6)	140.19 (C1')	130.16 (C4)	132.06 (Ci, vqn, J <sub>PCi</sub> + <sup>4</sup> J <sub>PCCPCi</sub> = 149.63 Hz)
129.19 (Ci, vq, J <sub>PCi</sub> + <sup>4</sup> J <sub>PCCPCi</sub> = 97.7 Hz)	129.30 (C4)	132.82 (Ci, d, J <sub>PCi</sub> = 107.2 Hz)	128.26 (C2' or C3')	131.28 (Cp, s)
129.15 (Cm, vt, <sup>3</sup> J <sub>PCm</sub> + <sup>6</sup> J <sub>PCCPCiCoCm</sub> = 11.5 Hz)	128.99 (Cm, vt, <sup>3</sup> J <sub>PCm</sub> + <sup>5</sup> J <sub>PCPCiCoCm</sub> = 12.0 Hz)	131.09 (Cp, d, <sup>4</sup> J <sub>PCp</sub> = 2.4 Hz)	127.49 (C2' or C3')	130.46 (C4)
124.30 (C1, vqn, <sup>3</sup> J <sub>PC1</sub> + <sup>6</sup> J <sub>PCCPNC2C1</sub> = 52.1 Hz)	128.31 (Ci, d, J <sub>PCi</sub> = 94.73 Hz)	130.72 (Co, d, <sup>2</sup> J <sub>PCo</sub> = 9.5 Hz)	63.13 (CH <sub>2</sub> N)	130.77 (Co, vt, <sup>2</sup> J <sub>PCo</sub> + <sup>5</sup> J <sub>PCCPCiCo</sub> = 9.7 Hz)
120.19 (C3, vt, <sup>3</sup> J <sub>PC3</sub> + <sup>6</sup> J <sub>PCCPNC2C3</sub> = 10.31 Hz)	124.65 (C1, vqn, <sup>3</sup> J <sub>PC1</sub> + <sup>5</sup> J <sub>PCPNC2C1</sub> = 42.0 Hz)	128.66 (Cm, d, <sup>3</sup> J <sub>PCm</sub> = 12.2 Hz)	48.75 (PhCH <sub>2</sub> N)	128.47 (Cm, vt, <sup>3</sup> J <sub>PCm</sub> + <sup>6</sup> J <sub>PCCPCiCoCm</sub> = 12.2 Hz)
117.55 (C5)	120.34 (C3, vt, <sup>3</sup> J <sub>PC3</sub> + <sup>5</sup> J <sub>PCPNC2C3</sub> = 11.9 Hz)	128.14 (C3')	23.39 (CH <sub>2</sub> P, vqn, J <sub>PC</sub> + <sup>3</sup> J <sub>PCCP</sub> = 125.8 Hz)	128.29 (C2' or C3')
51.61 (CH <sub>2</sub> N)	117.84 (C5)	125.83 (C4')	16.13 (CH <sub>3</sub> P, vqn, J <sub>PC</sub> + <sup>4</sup> J <sub>PCCPCH3</sub> = 127.3 Hz)	127.14 (C4')
23.34 (CH <sub>2</sub> P, vqn, J <sub>PC</sub> + <sup>3</sup> J <sub>PCCP</sub> = 102.8 Hz)	50.94 (CH <sub>2</sub> N)	125.10 (C2')	C4' was not observed	127.01 (C2' or C3')
C6 was not observed	26.56 (CH <sub>2</sub> P, t, J <sub>PC</sub> = 72.6 Hz)	104.37 (C4)		62.68 (CH <sub>2</sub> N)
		61.76 (CH <sub>2</sub> CH <sub>2</sub> N)		49.15 (PhCH <sub>2</sub> N)
		29.42 (CH <sub>2</sub> CH <sub>2</sub> N)		21.57 (CH <sub>2</sub> P, vqn, J <sub>PC</sub> + <sup>3</sup> J <sub>PCCP</sub> = 126.2 Hz)
		26.13 (CH <sub>2</sub> CH <sub>2</sub> P, d, J <sub>PC</sub> = 48.8 Hz)		
		21.69 (CH <sub>3</sub> CH <sub>2</sub> P, d, <sup>2</sup> J <sub>PC</sub> = 15.6 Hz)		
		14.07 (CH <sub>3</sub> )		

<sup>a</sup> The *J* for the virtual multiplet is the spacing between the two outer peaks. *Ci*, *Co*, *Cm* and *Cp* denote the carbon atoms of the phenyl substituents in the phosphine fragment. C1', C2', C3' and C4' refer to the carbon atoms of the phenyl and benzyl substituents at N1 of the heterocyclic ring in **8**, **11a** and **11b**. C1, C2, C3, C4, C5 and C6 denote the carbon atoms of the phenyl rings in compounds **4b** and **5**, C1 being the carbon atom linked to the methylene group, or the carbon atoms of the heterocyclic rings in compounds **8**, **11a** and **11b**.

5.84 ppm; MS (FAB<sup>+</sup>): 607.69 (M<sup>+</sup> + 1, 100). Anal. Found: C, 79.37; H, 5.78; N, 4.43. C<sub>40</sub>H<sub>36</sub>N<sub>2</sub>P<sub>2</sub> (606.69). Calc.: C, 79.19; H, 5.98; N, 4.62%.

Compound **4a**: yield 95%; m.p. 166–168 °C (colourless prisms from diethyl ether); IR (Nujol):  $\nu$  1596, 1482, 1328, 1119, 1055, 756, 742, 723, 696 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  7.58–7.10 (20H, m), 6.83–6.68 (6H, m), 6.23 (2H, d,  $J = 6.99$  Hz), 4.92 (4H, s), 2.68 (4H, s) ppm; <sup>13</sup>C NMR (CDCl<sub>3</sub>):  $\delta$  149.89, 133.30 (vt,  $J = 13.7$  Hz), 131.79 (C<sub>o</sub>, vt,  $J = 9.1$  Hz), 131.71 (C<sub>p</sub>, s), 130.96, 128.75 (C<sub>m</sub>, vt,  $J = 11.8$  Hz), 128.15, 124.04 (vt,  $J = 7.1$  Hz), 118.57, 70.94, 22.96 (CH<sub>2</sub>P, vqn,  $J = 113.3$  Hz) ppm (the C<sub>1</sub> was not observed); <sup>31</sup>P NMR (CDCl<sub>3</sub>):  $\delta$  5.92 ppm; MS (FAB<sup>+</sup>): 623.69 (M<sup>+</sup> + 1, 100). Anal. Found: C, 77.31; H, 5.71; N, 4.31. C<sub>40</sub>H<sub>36</sub>N<sub>2</sub>OP<sub>2</sub> (622.69). Calc.: C, 77.16; H, 5.83; N, 4.50%.

Compound **4b**: yield 91%; m.p. 248–250 °C (colourless prisms from dichloromethane–diethyl ether); IR (Nujol):  $\nu$  1594, 1484, 1537, 1334, 1109, 738, 720, 695 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  10.02 (1H, s), 7.65–7.37 (20H, m), 7.26 (2H, d,  $J = 7.33$  Hz), 6.81 (2H, td,  $J = 1.27, 7.61$  Hz), 6.59 (2H, t,  $J = 7.30$  Hz), 6.28 (2H, d,  $J = 7.89$  Hz), 4.25 (4H, s), 2.74 (4H, d,  $J_{PC} = 3.35$  Hz) ppm; MS (FAB<sup>+</sup>): 622.71 (M<sup>+</sup> + 1, 100). Anal. Found: C, 77.11; H, 5.89; N, 6.59. C<sub>40</sub>H<sub>37</sub>N<sub>3</sub>P<sub>2</sub> (621.71). Calc.: C, 77.28; H, 6.00; N, 6.76%.

Compound **5**: yield 97%; m.p. 317–319 °C (colourless prisms from chloroform–*n*-hexane); IR (Nujol):  $\nu$  1597, 1436, 1333, 1297, 1111, 775, 750, 739, 691 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  10.68 (1H, s), 7.64–7.55 (8H, m), 7.40–7.17 (14H, m), 6.81 (2H, td,  $J = 1.29, 7.56$  Hz), 6.62 (2H, t,  $J = 7.26$  Hz), 6.16 (2H, dm,  $J = 7.86$  Hz), 4.27 (4H, s), 3.74 (2H, t,  $J_{PH} = 13.03$  Hz) ppm; MS (FAB<sup>+</sup>): 608.68 (M<sup>+</sup> + 1, 100). Anal. Found: C, 77.20; H, 5.73; N, 6.79. C<sub>39</sub>H<sub>35</sub>N<sub>3</sub>P<sub>2</sub> (607.68). Calc.: C, 77.09; H, 5.81; N, 6.91%.

Compound **8**: yield 56%; m.p. 244–246 °C (colourless prisms from dichloromethane–diethyl ether); IR (Nujol):  $\nu$  1647, 1534, 1506, 1438, 1115, 747, 724, 696 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  7.78 (4H, d,  $J = 7.61$  Hz), 7.72 (2H, s), 7.62–7.52 (8H, m), 7.40–7.24 (18H, m), 2.84 (4H, broad s), 2.65 (4H, broad s), 2.43 (6H, s), 1.40 (8H, broad s); MS (FAB<sup>+</sup>): 878.03 (M<sup>+</sup> + 1, 21). Anal. Found: C, 73.79; H, 6.10; N, 12.89. C<sub>54</sub>H<sub>54</sub>N<sub>8</sub>P<sub>2</sub> (877.03). Calc.: C, 73.95; H, 6.21; N, 12.78%.

Compound **11a**: yield 41%; m.p. 164–165 °C (yellow prisms from dichloromethane–*n*-hexane); IR (Nujol):  $\nu$  1647, 1557, 1296, 1138, 1053, 934, 866, 724 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  8.44 (2H, s), 7.28–7.10 (10H, m), 5.23 (4H, s), 3.70 (4H, s), 2.07 (4H, d,  $J_{PH} = 2.45$  Hz), 1.28 (12H, vt,  $J = 12.17$  Hz) ppm; MS (FAB<sup>+</sup>): 575.61 (M<sup>+</sup> + 1, 16). Anal. Found: C, 58.38; H, 6.18; N, 24.17. C<sub>28</sub>H<sub>36</sub>N<sub>10</sub>P<sub>2</sub> (574.61). Calc.: C, 58.53; H, 6.32; N, 24.38%.

Compound **11b**: yield 39%; m.p. 239–240 °C (colourless prisms from ethanol); IR (Nujol):  $\nu$  1649, 1642, 1581, 1342, 1172, 1132, 1104, 1024, 752, 718, 701 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  8.07 (2H, s), 7.42–7.08 (30H, m), 5.52 (4H, s), 2.88 (4H, s), 2.87 (4H, d,  $J_{PH} = 2.63$  Hz) ppm; MS (FAB<sup>+</sup>): 823.90 (M<sup>+</sup> + 1, 27). Anal. Found: C, 70.22; H, 5.27; N, 16.91. C<sub>48</sub>H<sub>44</sub>N<sub>10</sub>P<sub>2</sub> (822.90). Calc.: C, 70.06; H, 5.39; N, 17.02%.

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