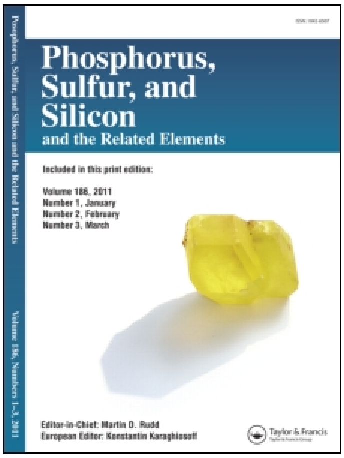

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PREPARATION AND CHROMATOGRAPHIC SEPARATION OF DIASTEREOISOMERIC DIAZA-DIPHOSPHA-MACROCYCLES

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PREPARATION AND CHROMATOGRAPHIC SEPARATION OF DIASTEREOISOMERIC DIAZA-DIPHOSPHA-MACROCYCLES

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Chiral macrocyclic binaphthyl derivatives, containing phosphorus and nitrogen hetero atoms, have been prepared as mixtures of three diastereoisomers. Their separation on a preparative scale was achieved after two chromatographic steps using polystyrene gel and strongly deactivated silica gel to avoid irreversible adsorption. A configurational assignment of the diastereoisomers was partly possible on the basis of NMR spectroscopy.

Key words: Gel chromatography, alane reduction (of haloamides), 1,1′-binaphthyls, chromatographic separation of diastereoisomers, diaza-diphospha-macrocycles.

INTRODUCTION

The frequently observed pronounced sensitivity of phosphorus(III) compounds towards oxidation together with their attractivity as (chiral) ligands in homogeneous catalysis makes the development of mild and efficient purification methods highly desirable.[1] As a consequence of increasing structural complexity the formation of several diastereoisomers, often in comparable quantities, cannot be suppressed, and a method for their separation on a preparative scale is required. Low-molecular weight diastereoisomeric phosphines have been separated in a number of cases by fractional crystallisation or via their transition metal complexes, however, these methods are not of general applicability.[2] Especially with larger molecules (m.w. >500 dalton) it has been proven to be difficult to induce crystallisation even when the samples are rather pure. For less sensitive compounds adsorption chromatography is usually the method of choice for the resolution of isomeric mixtures. Silica gel, the most wildly used adsorbent with high capacity and good selectivity, tends to oxidise phosphines and/or adsorb them irreversibly, thus resulting in a dramatic decrease of the chemical yield.[3]

Here we report the synthesis of three chiral macrocyclic binaphthyl derivatives with phosphorus and nitrogen complexation sites and with different degrees of chemical stability. All of them are obtained as mixture of three diastereoisomers which were baseline separated or highly enriched by two chromatographic steps. A size exclusion chromatography was applied to isolate the isomers from educts and unidentified side products. A subsequent adsorption chromatography using silica gel with high but defined water content afforded pure or highly enriched fractions of the diastereoisomers.

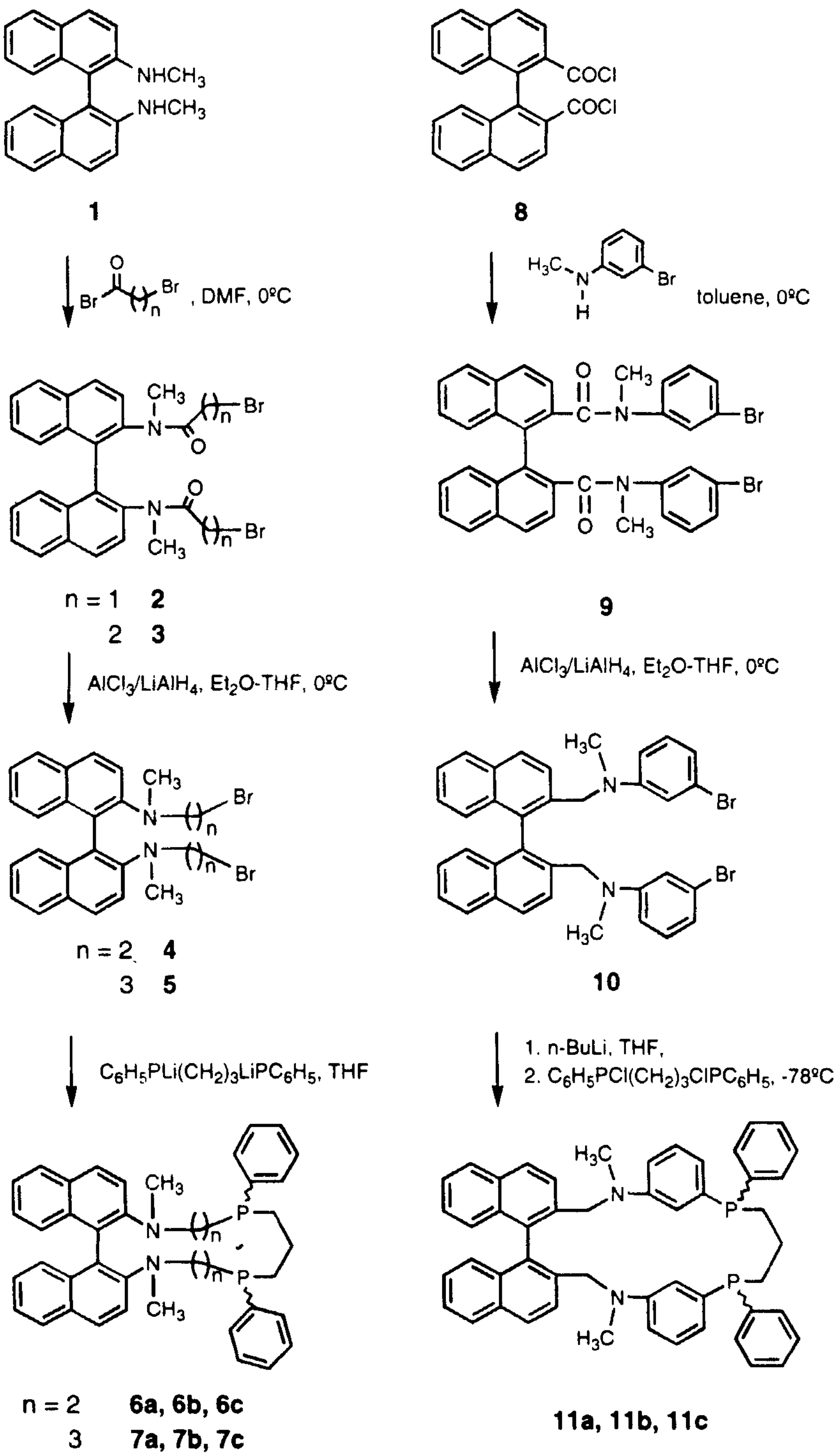
RESULTS AND DISCUSSION

During the course of our investigations on the conformation of macrocyclic binaphthyl-based diphosphines,[4] we were interested in the preparation of diazadiphospha compounds like **6**, **7**, and **11** in order to find appropriate structures suitable as chiral auxiliaries in asymmetric catalysis (Scheme I). Atropisomeric 2,2′-bis(diphenylphosphino)-1,1′-binaphthyl (BINAP) and structurally related ligands revealed high enantioselectivities in a large number of exemplary catalytic reactions.[5,6] From this reason a modification of the steric interactions, as effected by the implementation of the binaphthyl subunit into a cyclic structure, is expected to change reactivity and eventually enhance the enantioselectivity of asymmetric syntheses.

Besides 2,2′-dihydroxy-1,1′-binaphthyl 2,2′-diamino-1,1′-binaphthyl and 1,1′-binaphthyl-2,2′-dicarboxylic acid seem to be suitable precursors, especially if the preparation of optically active compounds is intended. Therefore we have set out to prepare macrocycles of different size and flexibility as depicted in Scheme I.

The *Synthesis of Macrocycles* **6**, **7**, and **11** was conducted in three steps; 1) two spacer groups of a suitable length and difunctionality were attached to the binaphthyl precursor; 2) conversion of functional groups; 3) cyclisation reactions with a suitable diphosphine, like 1,3-bis(phenylphosphino)propane. This strategy resulted in the formation of three diastereoisomers, since two chiral phosphorus centers were introduced.

2,2′-Bis(methylamino)-1,1′-binaphthyl (**1**) was accessible from 2-hydroxynaphthaline in three steps according to known procedures.[7] Numerous attempts have been made to introduce C_2 or C_3 fragments at nitrogen by alkylation with 3-bromo-, 3-chloro-1-propanol, 1-bromo-3-chloropropane, trimethyleneoxide, and oxirane under various conditions. Under mild conditions either no conversion or the slow formation of monoalkylated products was observed (up to 40% with K_2CO_3 after 100 h in refluxing EtOH/benzene), while the usage of stronger bases and/or prolonged heating resulted in considerable decomposition. In no case dialkylated products could be detected. An alternative route to 2,2′-bis(N-2-bromoethyl-N-methylamino)-1,1′-binaphthyl (**4**) and 2,2′-bis(N-3-bromopropyl-N-methylamino)-1,1′-binaphthyl (**5**) via twofold amide formation required a selective reduction method for **2** and **3** which would tolerate bromo substituents. Various reagents have been investigated including BH_3-THF,[8] BH_3-DMS,[9] and $LiAlH_4/AlCl_3$ ("AlH_3").[10] The latter one was found to be the reagent of choice, since the reaction proceeded smoothly at 0°C and afforded **4** and **5** in 84% and 52% yields, respectively. An extension to C_4-fragments failed because of the pronounced tendency of intramolecular quarternation. FAB-MS and NMR evidences pointed to a pyrrolidinium structure. **4** and **5** were treated with equimolar amounts of the dilithio salt of 1,3-bis(phenylphosphino)propane in dry THF at RT in moderate dilution. Extractive workup and size exclusion chromatography yielded a mixture of diastereoisomers **6a–c** and **7a–c**, respectively, as pale yellow foams. The synthesis of cycle **11** was conducted similarly; dichloride **8**[11] was treated with excess of 3-bromo-N-methyl-aniline (toluene, 0°C) to give **9** (93%). Also in this case the reduction to amine **10** was best accomplished with "AlH_3" ($LiAlH_4/AlCl_3$, 90%). Other reagents were less satisfying (BH_3-THF, 48%; $NaBH_4/TiCl_4$,[12] 77%). The cycli-


NHCH3
NHCH3
1
COCl
COCl
8
Br, DMF, 0ºC
n
toluene, 0ºC
H3C
N
H
Br
n = 1 2
2 3
9
AlCl3/LiAlH4, Et2O-THF, 0ºC
AlCl3/LiAlH4, Et2O-THF, 0ºC
n = 2 4
3 5
10
C6H5PLi(CH2)3LiPC6H5, THF
1. n-BuLi, THF,
2. C6H5PCl(CH2)3ClPC6H5, -78ºC
n = 2 6a, 6b, 6c
3 7a, 7b, 7c
11a, 11b, 11c

SCHEME I

sation of the dilithium derivative of **10**, prepared by double metal-halogen exchange with *n*-BuLi at −78°C, with 1,3-bis(chlorophenylphosphino)propane proceeded at low temperature without dilution.

Separation of Diastereoisomers

The crude reaction mixture was subjected to column chromatography on cross-linked polystyrene gel in CH_2Cl_2 in order to separate low-molecular weight by-products (i.e. partly oxidized 1,3-bis(phenylphosphino)propane) and oligomeric products from the desired macrocycles. The obtained mixture of diastereoisomers was separated on silica gel which contained a defined amount of water. This had to be adjusted carefully as too low water content leads to irreversible adsorption of the products and consequently poor and irreproducible yields, while a too high

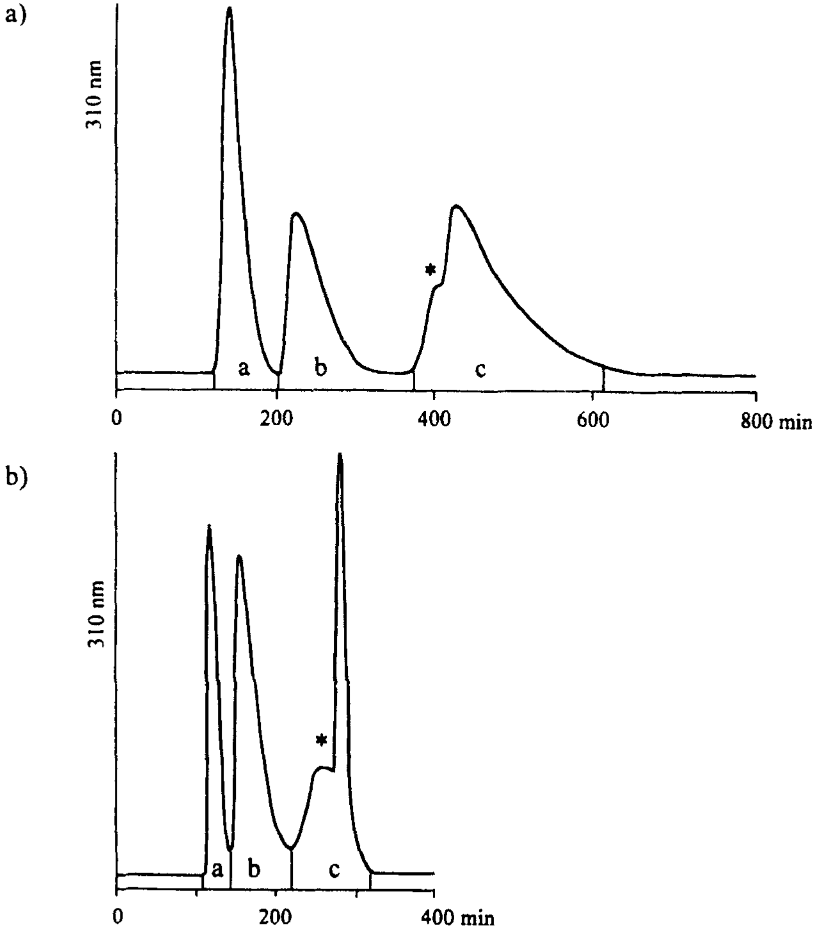


FIGURE 1 Chromatographic separation of diastereomers of **6a–c** on silica gel. Column: 50 × 2 cm, CH_2Cl_2/petroleum ether (40:60); the asterisk (*) indicates a solvent change: CH_2Cl_2/petroleum ether (50:50) or CH_2Cl_2; a) silica gel, 12% (w/w) water, sample 349 mg, total recovery: 140 mg (40%); b) silica gel, 23% (w/w) water, sample 350 mg, total recovery: 203 mg (58%).

TABLE I

Chromatographic purification of stereoisomeric macrocycles

Compound	Symmetry	after gel chromatography[a)]		after adsoption chromatography[a)]	
		calcd. yield [%][b)]	isomeric ratio[b)]	isolated yield [%]	isomeric ratio
6a	C_2	10	14	9	25
6b	C_1	36	53	13	36
6c	C_2	22	33	14	39
7a	C_2	10	31	4	40
7b	C_2	6	18	c)	—
7c	C_1	17	51	c)	—
11a	C_2	4	20	3	20
11b	C_1	13	57	8	56
11c	C_2	5	23	3	24

[a] For chromatographic conditions see Experimental Section.

[b] Calculated from ^{31}P NMR integration using a relaxation delay of 10 s.

[c] Only enriched fraction of **7b** and **7c** (approximately 80%) could be obtained to give an overall yield of 6%.

content results in poor separation efficiency. Besides the activity of the adsorbent also the sample load and the column length affected the total amount of recovered material and its composition. For each case optimized conditions had to be found by trial and error (see Experimental Section). As a typical example the separation of **6a–c** is depicted in Figure 1 demonstrating the effect of the varying amounts of water. Silica gel deactivated with 12% of water resulted in a recovery rate of 40%, whereas a water content of 23% improved the overall yield to 58%.

The use of other additives like methanol or triethylamine instead of water resulted in too high deactivation. Table I compares yields of diastereoisomers obtained before and after adsorption chromatography and shows influence of water content and sample load on the selectivity and recovery rate. This behavior reflects the different reactivity of phosphorus lone pairs and can be rationalized in terms of steric (relative configuration of phosphorus atoms, flexibility of the macrocyclic perimeter) and electronic effects (Ar_2RP vs. ArR_2P).

The described procedure was found to be a convenient and simple method for the resolution of complex mixtures of chemically labile compounds since it needs no special equipment and seems to be of general applicability. So it will be of value especially if only small but pure samples for the characterisation (NMR experiments, X-ray structural analyses, chiroptical properties, etc.) or preliminary experiments (asymmetric catalysis) are required.

EXPERIMENTAL

Melting points: Kofler Heiztisch-Mikroskop, uncorrected; NMR: AC 250 F, AM 400 WB (Bruker); spectra were recorded in $CDCl_3$ at 400.1 MHz (^1H), 100.6 (^{13}C, *J*-modulated), and 162.0 MHz (^{31}P, proton decoupled), respectively, if not otherwise noted. Chemical shift δ are given relative to TMS (^{1}H, ^{13}C) and 85% H_3PO_4 (^{31}P). In ^{13}C NMR spectra *J* refers to phosphorus-carbon-coupling constants which were identified by comparison of spectra recorded at 62.9 and 100.6 MHz. In areas of extensive signal overlapping no assignment could be made. These CH-signals of unclear relationship are underlined ignoring multiplett patterns.

MS: Varian MAT-CH7; elemental analyses: Mikroanalytisches Laboratorium der Universität Wien.

THF was distilled from potassium benzophenone ketyl, Et_2O from $LiAlH_4$. DMF was distilled and stored over molecular sieves 4 Å petroleum ether (PE, b.p.: 60–70°C) was used as purchased; ethyl acetate (AcOEt), CH_2Cl_2, chlorodiphenylphosphine, and m-bromoaniline were distilled. All other chemicals were analytical grade. TLC: aluminium sheets, silica gel 60, F_{254} (Merck). Adsorption chromatography: Silica gel 60, 230–400 mesh ASTM (Merck); for the separation of diastereoisomers silica gel was kept for two days at 140–160°C. The adsorbent was transferred to a flask and a calculated amount of water was added. The flask was stoppered and after vigorous shaking was allowed to stand for at least 2 days in order to become homogeneous. For the size-exclusion chromatography crosslinked polystyrene was used (3% divinylbenzene; Bio-Beads® S-X3, 200–400 mesh, (Bio Rad), column: 2.5 × 75 cm. Reactions involving AlH_3 or organolithium compounds were performed under a dry atmosphere of Ar using Schlenk technique.

The following compounds were prepared according to reported procedures: 2,2′-diamino-1,1′-binaphthyl,[7] 1,1′-binaphthyl-2,2′-dicarbonylchloride,[11] 3-bromo-*N*-methylaniline,[13] 3-bromo-propionylbromide,[14] 1,3-bis(phenylphosphino)propane,[15] 1,3-bis(chlorophenylphosphino)propane.[16]

Preparation of 2,2′-Bis[N-(2-bromomethylcarbonyl)-N-methyl-amino]-1,1′-binaphthyl (**2**) *and 2,2′-Bis-[N-(3-bromoethylcarbonyl)-N-methyl-amino]-1,1′-binaphthyl* (**3**) *(General Procedure)*: 1.53 ml (17.6 mmol, 2.2 equiv.) of 2-bromoacetylbromide or 1.86 ml (17.6 mmol, 2.2 equiv.) of 3-bromopropionylbromide, respectively, were added dropwise to a solution of 2.50 g (8.0 mmol) of 2,2′-bis(N-methylamino)-1,1′-binaphthyl (**1**) in 25 ml of dry DMF at 0°C. After stirring for 1 h the mixture was diluted with Et_2O and water was added. Stirring was continued for 30 min at RT to destroy excess of acylbromides. The organic phase was separated and the aqueous one was extracted twice with Et_2O. The combined organic extracts were washed with brine and dried with Na_2SO_4.

2: When the organic layer was concentrated to ca. 90 ml crystallisation of amide **2** started. The crystals were collected, washed with Et_2O/hexane and dried in vacuo to give 2.93 g (66%) of **2**. The mother liquor was concentrated and flashed over silica gel (PE/AcOEt 80:20 → 70:30) to give a second crop of product; total yield: 3.77 g (85%) of **2**; m.p.: 139–142°C. On the basis of ^{1}H NMR integration a ratio of conformers 71(A):29(B) was calculated. ^{1}H NMR: δ 2.62^{A} (s, 4.2H), 2.66^{B} (s, 1.8H), 3.58^{B} (AB-system, 0.6H, ^2J 10.9 Hz), 3.70^{B} (AB-system, 0.6H, *J* 11.0 Hz), 3.74^{A} (A′B′-system, 1.4H, *J* 11.2 Hz), 3.89^{A} (A′B′-system, 1.4H, *J* 11.1 Hz), 6.88^{B} (d, 0.6H, *J* 8.4 Hz), 7.06^{A} (d, 1.4H, *J* 8.5 Hz), 7.27^{A} (m, 1.4H), 7.31^{B} (m, 0.6H), 7.49^{A} (m, 1.4H), 7.50^{A} (d, 1.4H, *J* 8.8 Hz), 7.54^{B} (m, 0.6H), 7.76^{B} (d, 0.6H, *J* 8.6 Hz), 7.95^{A} (d, 1.4H, *J* 8.2 Hz), 7.99^{A} (d, 1.4H, *J* 8.8 Hz), 7.80^{B} (d, 0.6H, *J* 8.1 Hz), 8.12^{B} (d, 0.6H, *J* 8.7 Hz); ^{13}C NMR: δ 26.76^{B} (CH_2), 28.59^{A} (CH_2), 36.52^{B} (CH_3), 38.02^{A} (CH_3), 125.50^{B} (CH), 125.94^{A} (CH), 126.08^{B} (CH), 126.22^{A} (CH), 126.90^{A} (CH), $127{:}06^{B}$ (CH), 127.13^{A} (CH), 127.94^{B} (CH), 128.33^{A} (CH), 128.54^{B} (CH), 128.80^{A} (C), 129.21^{A} (CH), 129.85^{B} (C), 130.87^{B} (CH), 132.28^{A} (C), 132.64^{B} (C), 133.39^{A} (C), 133.62^{B} (C), 139.41^{B} (C), 140.98^{A} (C), 167.62^{B} (C), 168.42^{A} (C); MS (170°C): 552 (M^+, ^{79}Br, 4%); analysis calcd. for $C_{26}H_{22}Br_2N_2O_2$: C 56.34, H 4.00, N 5.05, found: C 56.15, H 4.22, N 5.01.

3: Removal of the solvent gave a yellow foam which was used in the next reaction without further purification; yield: 4.10 g (88%) of **3**. ^{1}H NMR integration showed conformers in a ratio 43(A):57(B). ^{1}H NMR: δ 2.45^{A} (ddd, 1 H, *J* 4.4, 6.9, 11.3), 2.50^{B} (s, 3 H), 2.68^{A} (s, 3H), $2.75–2.89^{B}$ (m, 2H), 3.03^{A} (m, 1H), $3.48^{A,B}$ (m, 2H), 3.68^{B} (m, 1H), 3.77^{A} (m, 1H), 6.75^{A} (d, 1H, *J* 8.4 Hz), 7.07^{B} (d, 1H, *J* 8.4 Hz), $7.24^{A,B}$ (m, 2H), 7.46^{B} (m, 1H), 7.48^{A} (m, 1H), 7.50^{B} (d, 1H, *J* 8.9 Hz), 7.56^{A} (d, 1H, *J* 8.9 Hz), 7.92^{B} (d, 1H, *J* 7.9 Hz), 7.94^{A} (d, 1H, *J* 8.4 Hz), 7.95^{B} (d, 1H, *J* 7.9 Hz), 8.05^{A} (d, 1H, *J* 8.9 Hz); ^{13}C NMR: δ 27.38^{B} (CH_2), 27.58^{A} (CH_2), 35.57^{A} (CH_3), 36.86^{B} (CH_2), 37.06^{A} (CH_2), 37.56^{B} (CH_3), $126.02^{B,B}$ (2CH), 126.12^{A} (CH), 126.76^{B} (CH), 126.80^{A} (CH), 127.38^{A} (CH), 127.63^{A} (CH), 127.87^{B} (CH), 128.30^{B} (CH), 128.36^{B} (CH), 128.93 (C), 129.05^{A} (CH), 130.40^{A} (CH), 132.18 (C), 132.45 (C), 133.50 (C), 133.93 (C), 139.13 (C), 141.47 (C), 171.20 (C), 171.81 (C); MS (160°C): 580 (M^+, ^{79}Br, 13%); HRMS: calcd. for $C_{28}H_{26}Br_2N_2O_2$: 580.0361; found 580.0369.

Preparation of 2,2′-Bis[N-(2-bromoethyl)-N-methylamino]-1,1′-binaphthyl (**4**) *and 2,2′-Bis-[N-(3-bromopropyl)-N-methylamino]-1,1′-binaphthyl* (**5**) *(General Procedure)*: A suspension of 490 mg (12.9 mmol) of $LiAlH_4$ in 140 ml of dry Et_2O was cooled with an ice/salt mixture. 573 mg (4.3 mmol) of $AlCl_3$ was added carefully, and the mixture was stirred for 20 min. To the resulting white suspension was added a solution of 3 mmol of amide (1.66 g of **2**, 1.75 g of **3**) in 10 ml of THF. The degree of conversion was monitored via TLC (R_f **4**: 0.47; **5**: 0.59 in PE/AcOEt 95:5). When no educt could be detected (usually after 10 min) the reaction was quenched by careful addition of water. The organic layer was separated and the aqueous one was sufficiently extracted with Et_2O. The combined organic extracts were washed with water and brine and dried with Na_2SO_4. The solvent was removed in vacuo.

4: The product was isolated as an oil which crystallized after prolonged drying in vacuo; yield: 1.48 g (94%) of **4**. Since we noticed a pronounced tendency of **4** to decompose on SiO_2 or if stored for longer periods, it was immediately used in the next step after sufficient drying (10 h, 0.05 torr). An analytically pure sample was obtained after chromatography (SiO_2, CH_2Cl_2). ^1H NMR: δ 2.38 (m, 2H), 2.70 (s, 6H), 2.77 (m, 2H), 2.94 (m, 4H), 7.13 (d, 2H, *J* 8.4 Hz), 7.21 (m, 2H), 7.35 (m, 2H), 7.50 (d, 2H, *J* 8.9 Hz), 7.86 (d, 2H, *J* 8.4 Hz), 7.93 (d, 2H, *J* 8.9 Hz); ^{13}C NMR: δ 29.10 (CH_2), 40.56 (CH_3), 58.04 (CH_2), 120.82 (CH), 124.13 (CH), 125.64 (CH), 126.50 (CH), 127.18 (C), 127.97 (CH), 128.85 (CH), 130.19 (C), 134.26 (C), 148.54 (C); analysis calcd. for $C_{26}H_{26}Br_2N_2$: C 59.33, H 4.98, N 5.32; found: C 59.87, H 4.84, N 5.33.

5: The crude oil was purified by chromatography in two runs (2 × 70 g SiO_2, PE/AcOEt 95:5); yield: 865 mg (52%) of **5**. An analytical sample was obtained by recrystallisation from CH_2Cl_2/Et_2O; m.p.: 108–110°C. ^1H NMR: δ 1.25 (m, 2H), 1.55 (m, 2H), 2.32 (m, 2H), 2.50–2.67 (m, 6H), 2.61 (s, 6H), 7.12 (d, 2H, *J* 8.4 Hz), 7.17 (t, 2H, *J* 7.8 Hz), 7.31 (t, 2H, *J* 7.9 Hz), 7.50 (d, 2H, *J* 8.9 Hz), 7.84 (d, 2H, *J* 8.1 Hz), 7.91 (d, 2H, *J* 8.9 Hz); ^{13}C NMR: δ 30.63 (CH_2), 31.01 (CH_2), 40.47 (CH_3), 55.63 (CH_2), 121.01 (CH), 123.97 (CH), 126.02 (CH), 126.15 (CH), 127.91 (CH), 128.16 (C), 128.63 (CH), 130.27 (C), 134.32 (C), 149.79 (C); MS (170°C): 552 (M^+, ^{79}Br, 4%); analysis calcd. for $C_{28}H_{30}Br_2N_2$: C 60.67, H 5.45, N 5.05; found: C 61.35, H 5.59, N 4.92.

1,11-Dimethyl-4,8-diphenyldinaphtho[*2,1-l:1′,2′-n*]*-1,11-diaza-4,8-diphosphacyclopentadeca-12,14-diene* (**6a–c**) *and 1,13-Dimethyl-5,9-diphenyldinaphtho*[*2,1-n:1′,2′-p*]*-1,13-diaza-5,9-diphosphacycloheptadeca-14,16-diene* (**7a–c**) *(General Procedure)*: To a solution of 333 μl (1.2 mmol) of 1,3-bis(phenylphosphino)propane in 20 ml of dry THF prepared in a Schlenk tube (A) was added 1.5 ml (2.4 mmol) of *n*-BuLi (1.6 molar solution in *n*-hexane) by a syringe at RT and the yellow solution was stirred for 20 min. In a second Schlenk tube (B) 1 mmol of dibromide (526 mg of **4**, 554 mg of **5**) were dissolved in 18 ml of THF. Finally a third Schlenk tube (200 ml, C) with a magnetic stirring bar was charged with 100 ml of THF. All Schlenk tubes were equipped with rubber septa. Two teflon cannula of same length and size (0.3 mm inner diameter) were used to connect Schlenk tubes (A) with (C) and (B) with (C). Schlenk tube (C) was connected to a bubbler and solutions of (A) and (B) were added slowly and synchronously over approximately 1.5 h with vigorous stirring into (C). The appropriate drop rate was easily adjusted by applying a small positive Ar pressure and by moving (A) and (B) up or down. At the end of the addition a few drops of dilithium phosphide was added in excess and the orange solution was stirred for 1 h. Since products were found to be sufficiently stable towards oxidation workup was conducted without precautions. The solvent was removed under vacuo and water was added. The mixture was extracted several times with CH_2Cl_2 and the combined extracts were washed with water and brine and dried with Na_2SO_4. After concentration the residue was treated as described below.

6: The crude mixture of products was chromatographed on cross-linked polystyrene in CH_2Cl_2 to give 423 mg (67%) of **6** as a mixture of three diastereoisomers. The separation was performed on deactivated SiO_2 (70 g, 22% (w/w) H_2O) with PE/CH_2Cl_2 (60:40 → 0:100) to yield **6a–c** as white foams.

6a: yield: 56 mg (9%); ^1H NMR: δ 1.71 (m, 6H), 1.86 (m, 2H), 2.04 (m, 2H), 2.20 (s, 6H), 3.24 (m, 4H), 7.15 (m, 4H), 7.31 (m, 8H), 7.44 (m, 4H), 7.59 (d, 2H, *J* 8.9 Hz), 7.84 (d, 2H, *J* 7.9 Hz), 7.93 (d, 2H, *J* 8.9 Hz); ^{13}C NMR: δ 21.49 (CH_2, t, *J* 12.8 Hz), 27.57 (CH_2, d, *J* 14.1 Hz), 29.30 (CH_2, t, *J* 11.8 Hz), 40.93 (CH_3), 54.26 (CH_2, d, *J* 29.5 Hz), 121.53 (CH), 123.71 (CH), 125.89 (CH), 126.26 (CH), 127.46 (C), 127.74 (CH), 128.33 (CH, d, *J* 6.8 Hz), 128.33 (CH), 128.58 (CH), 130.10 (C), 131.64 (CH, d, *J* 18.3 Hz), 134.63 (C), 139.77 (C, d, *J* 12.2 Hz), 150.36 (C); ^{31}P NMR: δ −29.1 (s); MS (240°C): 624 (M^+, 34%); analysis calcd. for $C_{41}H_{42}N_2P_2$: C 78.82, H 6.78, N 4.48, P 9.92; found: C 78.59, H 6.69, N 4.43, P 9.76.

6b: 79 mg (13%); white foam; ^1H NMR: δ 1.50–1.92 (m, 10H), 2.33 (s, 3H), 2.40 (s, 3H), 2.97 (m, 1H), 3.11–3.34 (m, 3H), 7.05 (d, 1H, *J* 8.4 Hz), 7.14 (m, 3H), 7.25–7.40 (m, 13H), 7.66 (d, 1H, *J* 8.9 Hz), 7.80 (d, 1H, *J* 7.9 Hz), 7.82 (d, 1H, *J* 7.9 Hz), 7.87 (d, 1H, *J* 8.9 Hz), 7.92 (d, 1H, *J* 8.9 Hz); ^{13}C NMR: δ 21.11 (CH_2, t, *J* 12.1 Hz), 25.61 (CH_2, d, *J* 17.8 Hz), 26.56 (CH_2, d, *J* 14.8 Hz), 27.58 (CH_2, dd, *J* 9.2, 14.5 Hz), 28.66 (CH_2, dd, *J* 10.3, 14.9 Hz), 40.53 (CH_3), 40.69 (CH_3), 51.54 (CH_2, d, *J* 16.3 Hz), 53.93 (CH_2, d, *J* 21.0 Hz), 121.46 (CH), 121.91 (CH), 123.57 (CH), 123.70 (CH), 125.75 (CH), 125.81 (CH), 126.15 (CH), 126.19 (CH), 126.69 (C), 126.97 (C), 127.64 (2CH), 127.90 (CH), 128.06 (CH), 128.21, 128.28, 128.32, 128.69, 129.64 (C), 130.10 (C), 131.24 (CH, d, *J* 19.2 Hz), 131.43 (CH, d, *J* 17.7 Hz), 134.21 (C), 134.85 (C), 139.60 (C, d, *J* 13.7 Hz), 139.88 (C, d, *J* 12.2 Hz), 148.68

(C), 150.04 (C); ^{31}P NMR: δ −28.9 (s), −26.2 (s); MS (240°C): 624 (M^+, 39%); analysis calcd. for $C_{41}H_{42}N_2P_2$: C 78.82, H 6.78, N 4.48, P 9.92; found: C 78.68, H 7.03, N 4.40, P 9.81.

6c: 88 mg (14%); ^{1}H NMR: δ 1.64–1.78 (m, 6H), 1.92 (m, 2H), 2.18 (m, 2H), 2.37 (s, 6H), 2.94 (m, 2H), 3.36 (m, 2H), 7.06 (d, 2H, *J* 8.4 Hz), 7.13 (m, 2H), 7.28–7.38 (m, 12H), 7.44 (d, 2H, *J* 8.9 Hz), 7.82 (d, 2H, *J* 8.4 Hz), 7.90 (d, 2H, *J* 8.9 Hz); ^{13}C NMR: δ 21.52 (CH_2, t, *J* 14.4 Hz), 25.60 (CH_2, d, *J* 17.3 Hz), 26.05 (CH_2, t, *J* 12.3 Hz), 41.21 (CH_3), 52.11 (CH_2, dd, *J* 2.3, 15.3 Hz), 121.42 (CH), 123.68 (CH), 125.59 (CH), 126.34 (CH), 127.56 (CH), 127.76 (C), 127.97 (CH), 128.23 (CH, d, *J* 6.2 Hz), 128.45 (CH), 130.04 (C), 131.37 (CH, d, *J* 17.4 Hz), 134.36 (C), 139.48 (C, d, *J* 13.6 Hz), 148.94 (C); ^{3}P NMR: δ −29.5 (s); MS (240°C): 624 (M^+, 44%); analysis calcd. for $C_{41}H_{42}N_2P_2$: C 78.82, H 6.78, N 4.48, P 9.92; found C 78.62, H 7.05, N 4.35, P 9.73.

7: Chromatography on polystyrene (see above) yielded: 215 mg (32%) of diastereoisomers **7a–c**. In the subsequent adsorption chromatography no baseline separation could be achieved; run I: sample 189 mg, (75 g SiO_2, 20%(w/w) H_2O) in PE/CH_2Cl_2 (65:35 → 60:40) gave 25 mg **7a** and 35 mg of **7b** + **c**; run II: sample 257 mg (40 g SiO_2, 10%(w/w) H_2O) in PE/CH_2Cl_2 (70:30 → 60:40) gave enriched fractions (ca. 80%) of **7b** and **7c**. Because of their limited stability towards oxidation characterisation was only made by ^{13}C and ^{31}P NMR spectra.

7a: ^{13}C NMR: δ 21.96 (CH_2, t, *J* 13.0 Hz), 23.31 (CH_2, d, *J* 12.8 Hz), 24.43 (CH_2, d, *J* 16.6 Hz), 29.46 (CH_2, dd, *J* 10.9 Hz, 13.4 Hz), 40.92 (CH_3), 57.17 (CH_2, d, *J* 12.4 Hz), 121.47 (CH), 123.74 (CH), 125.89 (CH), 126.37 (CH), 127.72 (CH), 128.04 (C), 128.17 (CH), 128.20 (CH, d, *J* 7.0 Hz), 128.54 (CH), 130.18 (C), 131.67 (CH, d, *J* 17.8 Hz), 134.82 (C), 139.73 (C, d, *J* 13.0 Hz), 149.68 (C); ^{31}P NMR: δ −25.3 (s); MS (270°C): 652 (M^+, 34%).

7b: ^{13}C NMR: δ 23.36 (CH_2, t, *J* 17.5 Hz), 23.87 (CH_2, d, *J* 9.9 Hz), 24.16 (CH_2, d, *J* 14.4 Hz), 27.02 (CH_2, t, *J* 12.8 Hz), 41.83 (CH_3), 57.71 (CH_2, d, *J* 11.4 Hz), 120.55 (CH), 123.58 (CH), 125.92 (CH), 126.20 (CH), 127.79 (CH), 127.85 (C), 127.91 (CH), 128.20 (CH, d, *J* 6.2 Hz), 128.49 (CH), 130.13 (C), 131.39 (CH, d, *J* 17.3 Hz), 135.02 (C), 140.08 (C, d, *J* 13.5 Hz), 149.52 (C); ^{31}P NMR: δ −25.6 (s).

7c: ^{13}C NMR (62.90 MHz): δ 22.27 (CH_2, dd, *J* 11.5, 15.1 Hz), 22.68 (CH_2, d, *J* 12.0 Hz), 23.74 (CH_2, d, *J* 10.1 Hz), 24.59 (CH_2, d, *J* 15.1 Hz), 24.92 (CH_2, d, *J* 19.5 Hz), 28.18 (CH_2, dd, *J* 10.0, 14.6 Hz), 29.51 (CH_2, dd, *J* 10.8, 14.1 Hz), 40.90 (CH_3), 42.41 (CH_3), 57.29 (CH_2, d, *J* 11.1 Hz), 58.16 (CH_2, d, *J* 14.8 Hz), 123.56 (CH), 123.88 (CH), 125.86 (2CH), 126.17 (CH), 126.36 (CH), 127.66, 127.77, 127.85, 127.90, 128.01, 128.11, 128.23, 128.69 (CH), 128.91 (C), 129.86 (C), 130.52 (C), 131.19 (CH, d, *J* 17.0 Hz), 131.53 (CH, d, *J* 17.5 Hz), 134.78 (C), 134.84 (C), 139.80 (C, d, *J* 13.5 Hz), 139.94 (C, d, *J* 13.4 Hz), 148.85 (C), 150.18 (C), one (C) was not observed; ^{31}P NMR: δ −24.7 (s), −24.1 (s).

2,2′-Bis[(N-3-bromophenyl-N-methyl)aminocarbonyl]-1,1′-binaphthyl (**9**): 2.29 g (6.0 mmol) of 1,1′-binaphthyl-2,2′-dicarbonylchloride (**8**) was added in portions into a stirred solution of 4.50 g (24.2 mmol) of m-bromo-*N*-methylaniline in 50 ml of toluene at 0°C. After stirring for 1 h the solvent was removed. Extractive workup with CH_2Cl_2 was followed by chromatography (40 g SiO_2, PE/AcOEt 75:25 → 70:30) to yield 3.79 g (93%) of **9** as a foam which was dried at 80°C in vacuo. ^{1}H NMR (d_8-toluene, 250.13 MHz, 360K): δ 3.29 (s, 6H), 6.54 (t, 2H, *J* 8.0 Hz), 6.73 (d, 2H, *J* 8.0 Hz), 6.82 (d, 2H, *J* 8.6 Hz), 6.92 (m, 4H), 7.06 (s, 2H), 7.30 (t, 2H, *J* 8.1 Hz), 7.70 (d, 2H, *J* 8.5 Hz), 7.75 (d, 2H, *J* 8.3 Hz), 7.80 (d, 2H, *J* 8.6 Hz); ^{13}C NMR (d_6-DMSO, 62.90 MHz, 350K): δ 38.32 (CH_3), 120.71 (C), 124.35 (CH), 124.59 (CH), 125.65 (CH), 126.08 (CH), 126.73 (CH), 127.02 (CH), 127.26 (CH), 128.13 (CH), 128.27 (CH), 129.72 (CH), 132.30 (C), 132.55 (C), 132.68 (C), 133.91 (C), 144.62 (C), 168.18 (C=O); MS (200°C): 676 (M^+, ^{79}Br, 4%); analysis calcd. for $C_{36}H_{26}Br_2N_2O_2$: C 63.74, H 3.86, N 4.13; found: C 63.83, H 4.04, N 4.01.

2,2′-Bis[(N-3-bromophenyl-N-methyl)aminomethyl]-1,1′-binaphthyl (**10**): A suspension was prepared from 0.96 g (25.4 mmol, 4.3 equiv.) of $LiAlH_4$ in 180 ml of Et_2O and cooled to −5°C. After the addition of 1.13 g (8.5 mmol, 1.4 equiv.) of $AlCl_3$ the mixture was stirred for 20 min. A solution of 4.00 g (5.9 mmol) of **9** in 15 ml of THF was added dropwise using a teflon canular (10 min). The reduction was followed by TLC (R_f 0.36, PE/AcOEt 95:5). After complete conversion (ca. 10 min) water was added carefully. The Et_2O-phase was separated and the remaining milky suspension was extracted twice with Et_2O. The combined extracts were washed with water and brine and dried with Na_2SO_4. Removal of the solvent afforded 3.45 g, (90%) of **10** which was found to be pure enough for the cyclisation reaction. An analytically pure sample was obtained by recrystallisation from CH_2Cl_2/pentane; m.p.: 184–185°C. ^{1}H NMR: δ 2.84 (s, 6H), 4.05 (AB-system, 2H, *J* 17.3 Hz), 4.20 (AB-system, 2H, *J* 17.3 Hz), 6.43 (d, 2H, 8.3 Hz), 6.65 (s, 2H), 6.76 (d, 2H, *J* 7.9 Hz), 6.93 (t, 2H, *J* 8.1 Hz), 7.19 (d, 2H, *J* 8.4 Hz), 7.34 (t, 2H, *J* 8.3 Hz), 7.48 (m, 4H), 7.94 (d, 4H, *J* 8.5 Hz); ^{13}C NMR: δ 38.48 (CH_3), 55.27 (CH_2), 110.73

(CH), 114.89 (CH), 119.34 (CH), 123.39 (C), 124.74 (CH), 124.97 (CH), 125.94 (CH), 126.87 (CH), 128.34 (CH), 128.58 (CH), 130.25 (CH), 132.48 (C), 133.08 (C), 133.44 (C), 134.64 (C), 150.84 (C); MS (230°C): 648 (M^+ ^{79}Br, 0.5%); analysis calcd. for $C_{36}H_{30}Br_2N_2$: C 66.48, H 4.65, N 4.31; found C 66.26, H 4.35, N 4.24.

1,13-Dimethyl-5,9-diphenyldibenzo[bc:jk]dinaphtho[2,1-o:1′,2′-q]-1,13-diaza-5,9-diphosphacyclononadeca-2,10,15,17-tetraene (**11a–c**): A solution of 800 mg (1.2 mmol) of **10** in 45 ml of dry THF was cooled to −78°C and 1.61 ml of *n*-BuLi (1.6 molar in hexane, 2.1 equiv.) was added dropwise. After stirring the reaction mixture for 2 h 425 mg (1.3 mmol, 1.1 equiv.) of 1,3-bis(chlorophenylphosphino)propane was added. The yellow mixture was allowed to come to RT overnight. Similar workup as outlined above for **6** and **7** was followed by gel permeation chromatography on polystyrene to afford a mixture of **11a–c**. A subsequent separation of diastereoisomers on SiO_2 (60 g, 22%(w/w) H_2O) in PE/CH_2Cl_2 (70:30 → 60:40) gave **11a–c** as white foams.

11a: 28 mg (3%); ^{1}H NMR: δ 1.44 (m, 2H), 1.91–2.11 (m, 4H), 2.79 (s, 6H), 3.94 (AB-system, 2H, *J* 17.7 Hz), 4.58 (AB-system, 2H, *J* 17.7 Hz), 6.34 (m, 2H), 6.62 (br d, 2H, *J* 7.9 Hz), 7.02 (br d, 2H, *J* 12.3 Hz), 7.09 (t, 2H, *J* 7.9 Hz), 7.15 (d, 2H, *J* 8.4 Hz), 7.30 (m, 8H), 7.38–7.56 (m, 6H), 7.61 (d, 2H, *J* 8.4 Hz), 7.95 (d, 4H, *J* 8.9 Hz); ^{13}C NMR (62.90 MHz): δ 22.67 (CH_2, t, *J* 17.8 Hz), 29.90 (CH_2, pt, *J* 12.9 Hz), 37.71 (CH_3), 55.49 (CH_2), 111.58 (CH, br), 119.07 (CH, d, *J* 44.6 Hz), 119.67 (CH, d, *J* 3.0 Hz), 124.76 (2CH), 125.74 (CH), 126.58 (CH), 128.12 (CH), 128.19 (CH), 128.24 (CH, d, *J* 6.4 Hz), 128.53 (CH), 129.56 (CH, br), 132.17 (CH, d, *J* 17.3 Hz), 132.24 (C), 133.22 (2C), 135.88 (C, br), 138.11 (C, d, *J* 10.5 Hz), 139.72 (C, d, *J* 12.3 Hz), 149.88 (C, d, *J* 15.2 Hz); ^{31}P NMR: δ −13.8 (s); MS (300°C): 748 (M^+, 56%); HRMS: calcd. for $C_{51}H_{46}N_2P_2$: 748.3136; found 748.3141.

11b: 74 mg (8%); ^{1}H NMR: δ 1.51 (m, 2H), 1.73–2.06 (m, 4H), 2.77 (s, 3H), 2.90 (s, 3H), 3.34 (AB-system, 1H, *J* 18.0 Hz), 3.80 (A′B′-system, 1H, *J* 18.2 Hz), 3.85 (AB-system, 1H, *J* 18.0 Hz), 4.23 (A′B′-system, 1H, *J* 18.2 Hz), 6.35 (br s, 1H), 6.50 (m, 4H), 6.73 (m, 4H), 6.99 (m, 2H), 7.07 (d, 1H, *J* 8.4 Hz), 7.11 (d, 1H, *J* 8.4 Hz), 7.18 (t, 1H, *J* 7.9 Hz), 7.28 (m, 7H), 7.38–7.53 (m, 4H), 7.59 (d, 1H, *J* 8.4 Hz), 7.85 (d, 1H, *J* 8.4 Hz), 7.93 (d, 2H, *J* 8.4 Hz), 7.98 (d, 1H, *J* 7.9 Hz); ^{13}C NMR: δ 21.60 (CH_2, dd, *J* 7.0, 17.6 Hz), 28.62 (CH_2, dd, *J* 11.9, 14.7 Hz), 30.04 (CH_2, dd, *J* 8.0, 12.5 Hz), 37.21 (CH_3), 38.76 (CH_3), 55.13 (2CH_2), 111.48 (br CH), 112.33 (br CH), 115.80 (br CH), 120.05 (br CH), 120.21 (CH, d, *J* 46.2 Hz), 123.61 (CH, br d, *J* 42.2 Hz), 124.39 (CH), 124.46 (2CH), 124.55 (CH), 125.66 (CH), 125.69 (CH), 126.08 (CH), 126.36 (CH), 126.61 (CH), 127.78 (CH, d, *J* 4.5 Hz), 127.87 (CH), 128.05 (CH), 128.10 (CH), 128.18 (CH, d, *J* 5.7 Hz), 128.29 (CH), 128.53 (CH), 129.03 (CH, d, *J* 15.2 Hz), 129.65 (CH, d, *J* 2.1 Hz), 130.85 (CH, d, *J* 14.4 Hz), 131.83 (CH, d, *J* 16.6 Hz), 132.00 (C), 132.06 (C), 132.89 (C), 132.96 (C), 133.02 (C), 133.22 (C), 134.96 (C), 135.30 (C), 137.58 (C, d, *J* 13.0 Hz), 138.01 (C, d, *J* 13.7 Hz), 138.78 (C, d, *J* 10.1 Hz), 140.37 (C, d, *J* 12.7 Hz), 149.33 (C), 149.69 (C, d, *J* 15.6 Hz); ^{31}P NMR: δ −13.5 (s), −9.2 (s); MS (300°C): 748 (M^+, 50%); HRMS: calcd. for $C_{51}H_{46}N_2P_2$: 748.3136; found 748.3131.

11c: 29 mg (3%); ^{1}H NMR: δ 1.49 (m, 2H), 1.64 (m, 2H), 2.00 (m, 2H), 2.79 (s, 6H), 3.40 (AB-system, 2H, *J* 17.2 Hz), 3.60 (AB-system, 2H, *J* 17.2 Hz), 6.37 (br s, 2H), 6.59 (br d, 2H, *J* 7.9 Hz), 6.71 (m, 6H), 6.91 (m, 6H), 7.07 (d, 2H, *J* 8.4 Hz), 7.20 (m, 2H), 7.26 (m, 2H), 7.33 (br m, 2H), 7.47 (br t, 2H, *J* 7.9 Hz), 7.88 (d, 2H, *J* 8.9 Hz), 7.94 (d, 2H, *J* 7.9 Hz); ^{13}C NMR: δ 19.40 (CH_2, m), 28.19 (CH_2, dd, *J* 6.2, 15.8 Hz), 37.88 (CH_3), 54.86 (CH_2), 112.59 (CH), 116.75 (CH, d, *J* 2.9 Hz), 123.54 (CH, d, *J* 38.2 Hz), 124.56 (CH), 125.10 (CH), 125.70 (CH), 126.43 (2CH), 127.74 (CH, d, *J* 4.8 Hz), 128.10 (CH), 128.12 (CH), 129.19 (CH, d, *J* 14.1 Hz), 131.10 (CH, d, *J* 14.7 Hz), 132.08 (C), 133.07 (C), 133.23 (C), 135.00 (C), 137.47 (C, d, *J* 14.1 Hz), 137.81 (C, d, *J* 13.2 Hz), 149.16 (C, d, *J* 2.3 Hz); ^{31}P NMR: δ −9.6 (s); MS (300°C): 748 (M^+, 60%); HRMS: calcd. for $C_{51}H_{46}N_2P_2$: 748.3136; found 748.3128.

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