**SUPPORTING INFORMATION_I**

# Dearomatizing Anionic Cyclization of Phosphonamides. A Route to Phosphonic Acid Derivatives with Antitumor Properties

Gloria Ruiz-Gómez,[a] Andrés Francesch,[b] María José Iglesias,[a] Fernando López-Ortiz,*[,a] Carmen Cuevas,[b] and Manuel Serrano-Ruiz[c]

[a]*Área de Química Orgánica, Universidad de Almería, Carretera de Sacramento, 04120, Almería. Spain.*

[b] *PharmaMar S.A. Av. de los Reyes, 1, P.I. La Mina, 28770 Colmenar Viejo, Madrid, Spain.*

[c]*Área de Química Inorgánica, Universidad de Almería, Carretera de Sacramento, 04120, Almería. Spain.*

*flortiz@ual.es*

**Contents:**

General experimental conditions and characterization of **8-17**…….……S4

-

**Figure S1.** $^{1}$H NMR (bottom) (300.13 MHz) and $^{13}$C{$^{1}$H}(middle) and DEPT-135 (top) NMR spectra (75.47 MHz) of **8a** measured in $CDCl_3$……..……..…….S18

**Figure S2.** 2D gNOESY spectrum (300.13 MHz, mixing time 0.5 s) of **8a** and selected NOEs observed that confirm the assignment of the relative configuration of the stereogenic centers……..S19

**Figure S3.** $^{1}$H NMR (bottom) (500.13 MHz) and $^{13}$C{$^{1}$H}(middle) and DEPT-135 (top) NMR spectra (125.76 MHz) of the epimer of **8a** at the phosphorus atom measured in $CDCl_3$……...S19

**Figure S4.** $^{1}$H NMR (bottom) (300.13 MHz) and $^{13}$C{$^{1}$H}(middle) and DEPT-135 (top) NMR spectra (75.47 MHz) of **10a** measured in $CDCl_3$……..……..……...S20

**Figure S5.** 2D gNOESY spectrum (300.13 MHz, mixing time 0.5 s) of **10a** and selected NOEs observed that confirm the assignment of the relative configuration of the stereogenic centers……..S20

**Figure S6.** $^{1}$H NMR (bottom) (300.13 MHz) and $^{13}$C{$^{1}$H}(middle) and DEPT-135 (top) NMR spectra (75.47 MHz) of the epimer of **10a** at the phosphorus atom measured in $CDCl_3$……...S21

**Figure S7.** 2D gNOESY spectrum (300.13 MHz, mixing time 0.5 s) of the epimer of **10a** at the phosphorus atom and selected NOEs observed that confirm the assignment of the relative configuration of the stereogenic centers…….……S21

**Figure S8.** $^{1}$H NMR (bottom) (300.13 MHz) and $^{13}$C{$^{1}$H}(middle) and DEPT-135 (top) NMR spectra (75.47 MHz) of **10b** measured in $CDCl_3$……...S22

**Figure S9.** 2D gNOESY spectrum (300.13 MHz, mixing time 0.5 s) of **10b** atom and selected NOEs observed that confirm the assignment of the relative configuration of the stereogenic centers..……S22

**Figure S10.** $^{1}$H NMR (bottom) (300.13 MHz) and $^{13}$C{$^{1}$H}(middle) and DEPT-135 (top) NMR spectra (75.47 MHz) of the epimer of **10b** at the phosphorus atom measured in $CDCl_3$.……..S23

**Figure S11.** 2D $^{1}H\{^{31}P\},^{1}H\{^{31}P\}$ gNOESY spectrum (300.13 MHz, mixing time 0.5 s) of the epimer of **10b** at the phosphorus atom and selected NOEs observed that confirm the assignment of the relative configuration of the stereogenic centers…….……..……..……....S23

**Figure S12.** $^{1}H$ NMR (bottom) (300.13 MHz) and $^{13}C\{^{1}H\}$(middle) and DEPT-135 (top) NMR spectra (75.47 MHz) of **9aa** measured in $CDCl_3$ at 55 ºC…..…….S24

**Figure S13.** 2D gNOESY spectrum (300.13 MHz, mixing time 0.5 s) at 55 ºC of **9aa** and selected NOEs observed that confirm the assignment of the relative configuration of the stereogenic centers.....S24

**Figure S14.** $^{1}H$ NMR (bottom) (300.13 MHz) at 60 ºC and $^{13}C\{^{1}H\}$(middle) and DEPT-135 (top) NMR spectra (75.47 MHz) at 22 ºC of **9ab** measured in $CDCl_3$...……S25

**Figure S15.** 2D $^{1}H\{^{31}P\},^{1}H\{^{31}P\}$ gNOESY spectrum (300.13 MHz, mixing time 0.5 s) at 60 ºC of **9ab** and selected NOEs observed that confirm the assignment of the relative configuration of the stereogenic centers……...S25

**Figure S16.** $^{1}H$ NMR (bottom) (300.13 MHz) and $^{13}C\{^{1}H\}$(middle) and DEPT-135 (top) NMR spectra (75.47 MHz) of **9ba** measured in $CDCl_3$ at 60 ºC…….……S26

**Figure S17.** 2D gNOESY spectrum (300.13 MHz, mixing time 0.5 s) at 60 ºC of **9ba** and selected NOEs observed that confirm the assignment of the relative configuration of the stereogenic centers……S26

**Figure S18.** $^{1}H$ NMR (bottom) (300.13 MHz) and $^{13}C\{^{1}H\}$(middle) and DEPT-135 (top) NMR spectra (75.47 MHz) of **9bb** measured in $CDCl_3$ at 55 ºC……....S27

**Figure S19.** 2D gNOESY spectrum (300.13 MHz, mixing time 0.5 s) at 55 ºC of **9bb** and selected NOEs observed that confirm the assignment of the relative configuration of the stereogenic centers……S27

**Figure S20.** $^{1}H$ NMR (bottom) (300.13 MHz) and $^{13}C\{^{1}H\}$(middle) and DEPT-135 (top) NMR spectra (75.47 MHz) of **9ca** measured in $CDCl_3$ at 60 ºC…….……S28

**Figure S21.** 2D gNOESY spectrum (300.13 MHz, mixing time 0.5 s) at 60 ºC of **9ca** and selected NOEs observed that confirm the assignment of the relative configuration of the stereogenic centers……...…….S28

**Figure S22.** $^{1}H$ NMR (bottom) (300.13 MHz) and $^{13}C\{^{1}H\}$(middle) and DEPT-135 (top) NMR spectra (75.47 MHz) of **9cb** measured in $CDCl_3$ at 45 ºC…….…….…….S29

**Figure S23.** 2D gNOESY spectrum (300.13 MHz, mixing time 0.5 s) at 45 ºC of **9cb** and selected NOEs observed that confirm the assignment of the relative configuration of the stereogenic centers……..S29

**Figure S24.** $^{1}H$ NMR (bottom) (300.13 MHz) and $^{13}C\{^{1}H\}$(middle) and DEPT-135 (top) NMR spectra (75.47 MHz) of **9da** measured in $CDCl_3$ at 50 ºC……..…….S33

**Figure S25.** 2D gNOESY spectrum (300.13 MHz, mixing time 0.5 s) at 50 ºC of **9da** and selected NOEs observed that confirm the assignment of the relative configuration of the stereogenic centers……S33

**Figure S26.** $^{1}$H NMR (bottom) (300.13 MHz) and $^{13}$C{$^{1}$H}(middle) and DEPT-135 (top) NMR spectra (75.47 MHz) of **9da** measured in $CDCl_3$ at 50 ºC…….....S34

**Figure S27.** 2D gNOESY spectrum (300.13 MHz, mixing time 0.5 s) at 50 ºC of **9db** and selected NOEs observed that confirm the assignment of the relative configuration of the stereogenic centers……S34

**Figure S28.** $^{1}$H NMR (bottom) (300.13 MHz) and $^{13}$C{$^{1}$H}(middle) and DEPT-135 (top) NMR spectra (75.47 MHz) of **10c** measured in $CDCl_3$……...S35

**Figure S29.** 2D ROESY spectrum (300.13 MHz, mixing time 0.2 s) of **10c** measured in $CDCl_3$.....S35

**Figure S30.** $^{1}$H NMR (bottom) (300.13 MHz) and $^{13}$C{$^{1}$H}(middle) and DEPT-135 (top) NMR spectra (75.47 MHz) of the epimer of **10c** at the phosphorus atom measured in $CDCl_3$……...S36

**Figure S31.** 2D gNOESY spectrum (300.13 MHz, mixing time 0.5 s) of the epimer of **10c** at the phosphorus atom measured in $CDCl_3$……S36

**Figure S32.** $^{1}$H NMR (bottom) (300.13 MHz) and $^{13}$C{$^{1}$H}(middle) and DEPT-135 (top) NMR spectra (75.47 MHz) of **11** measured in $CDCl_3$…….S37

**Figure S33.** $^{1}$H NMR (bottom) (300.13 MHz) and $^{13}$C{$^{1}$H}(middle) and DEPT-135 (top) NMR spectra (75.47 MHz) of **12** measured in $CDCl_3$…….S37

**Figure S34.** 2D gNOESY spectrum (300.13 MHz, mixing time 0.5 s) of **12** and selected NOEs observed that confirm the assignment of the relative configuration of the stereogenic centers……..S38

**Figure S35.** $^{1}$H NMR (bottom) (300.13 MHz) and $^{13}$C{$^{1}$H}(middle) and DEPT-135 (top) NMR spectra (75.47 MHz) of **13** measured in $CDCl_3$…….S38

**Figure S36.** $^{1}$H NMR (bottom) (300.13 MHz) and $^{13}$C{$^{1}$H}(middle) and DEPT-135 (top) NMR spectra (75.47 MHz) of **14** measured in $CDCl_3$…….S39

**Figure S37.** 2D gNOESY spectrum (300.13 MHz, mixing time 0.5 s) of **14** and selected NOEs observed that confirm the assignment of the relative configuration of the stereogenic centers……..S39

**Figure S38.** $^{1}$H NMR (bottom) (300.13 MHz) and $^{13}$C{$^{1}$H}(middle) and DEPT-135 (top) NMR spectra (75.47 MHz) of **16** measured in $D_2O$…….……S40

**Figure S39.** $^{1}$H and $^{1}$H{$^{31}$P } NMR spectra (300.13 MHz) of phosphonic acid **17a** measured in $D_2O$……S40

**Figure S40.** $^{1}$H NMR (bottom) (500.13 MHz) and $^{13}$C{$^{1}$H}(middle) and DEPT-135 (top) NMR spectra (125.76 MHz) of **17b** measured in MeOH-$d_4$……...S41

X-Ray data of compound **9aa** (Figure S41, Tables S1-S6)…….……...……S41

X-Ray data of compound **9ab** (Figure S42, Tables S7-S12)……...……..S50

X-Ray data of compound **14** (Figure S43, Tables S13-S18)……..S65

*(See Supporting Information_II for pages S31 to S72)*

**General experimental conditions**. All reactions were carried out under a nitrogen atmosphere using Schlenk techniques. THF was distilled from sodium/benzophenone immediately prior to use. DMPU was distilled from KOH under reduced pressure and stored over molecular sieves (3Å). Commercial reagents were distilled prior to their use, except *s*BuLi. TLC was performed on Merck plates with aluminum backing and silica gel 60 $F_{254}$. For column chromatography silica gel 60 (40-63 μm) was used.

Melting points are uncorrected. Infrared spectra were obtained in KBr pellets. Mass spectra were determined by electron impact on a LC-MS apparatus. NMR spectra were recorder on a spectrometer working at a field of 7 T (or 11.7 T, specific in the text), using $CDCl_3$ as solvent. Chemical shifts are referred to internal tetramethylsilane for $^1$H (300.13 MHz or 500.13 MHz) and $^{13}$C (75.47 MHz or 125.76 MHz), and to external 85% $H_3PO_4$ for $^{31}$P (121.47 MHz or 202.46 MHz). 2D NMR correlation spectra (gCOSY, gNOESY, gHMQC and gHMBC) and selective 1D gTOCSY and gNOESY were acquired using standard software and processing routines implemented in the spectrometer.

**X-Ray**. Data were collected on a BRUKER Smart-Apex CCD area-detector diffractometer, using MoKα radiation (λ = 0.71073 Å). The intensities were measured using the ω scan method. No empirical absorption correction was applied. The structure was solved by direct methods (SIR97)[1] and refined by full-matrix least-squares on $F^2$ using SHELXTL97.[2] Anisotropic thermal factors were assigned to all the non-hydrogen atoms. All the diagrams were generated by using the SHELXTL 97 and ORTEP programs. Crystallographic data (excluding structure factors) for the structures in this paper have been deposited in the Cambridge Crystallographic Data Centre as supplementary publications nos. CCDC 689868, 691971 and 689593. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (Telephone, +44 01223 762910; e-mail, deposit@ccdc.cam.ac.uk).

**Antitumor assays**. Human-derived established cell lines used in this study were purchased from ATCC (American Type Culture Collection): A-549, human lung carcinoma (ATCC # CCL-185); HT-29, human colorectal adenocarcinoma (ATCC # HTB-38); and MDA-MB 231, human breast adenocarcinoma (ATCC # HTB-26). All cell lines are maintained in DMEM (Dulbecco's Modified Eagle's Medium) culture medium supplemented with 10% FBS (Fetal bovine serum), 2 mM L-glutamine and 100 Units/mL penicillin and streptomycin at 37 ºC and 5% $CO_2$. Triplicate cultures were incubated for 72 hours in the presence or absence of test compounds (at 10 concentrations typically ranging from 10 to 0.0026 μg/mL).

A colorimetric assay using sulforhodamine B (SRB) has been adapted for a quantitative measurement of cell growth and viability, following a previously described method. Cells are plated

in 96-well microtiter plates at a density of $5x10^3$/well and incubated for 24 hours. One plate from each different cell line is fixed and stained, and used for Tz reference (see next paragraph). After that, cells are treated with vehicle alone (control) or compounds at the concentrations indicated. Treated cells are further incubated for 72 hours and cytotoxic evaluation performed by colorimetric analysis.

In brief, cells are washed twice with phosphate buffered saline (PBS), fixed for 15 min in 1% glutaraldehyde solution, rinsed twice in PBS, and stained in 0.4% SRB solution for 30 min at room temperature. Cells are then rinsed several times in 1% acetic acid solution and air-dried. SRB was then extracted in 10 mM trizma base solution and the absorbance measured at 490 nm. Cell survival is expressed as percentage of control cell growth.

Dose-response curves are performed by using the NCI algorithm.[3]

Tz= number of control cells at time $t_0$

C= number of control cells at time t

T= number of treated cells at time t

If **Tz < T < C** (Growth inhibition) then: **100*([T-Tz]/[C-Tz])**

If **T < Tz** (Net cell killing) then: **100*([T-Tz]/Tz)**

*After dose-curve generation, the following parameters are calculated by interpolation:*

**$GI_{50}$**: Concentration that causes 50% growth inhibition.

**TGI**: Concentration that causes total growth inhibition.

**$LC_{50}$**: Concentration that causes 50% net cell killing.

**General procedure for the synthesis of arylphosphonamides**.

To a solution of *N*-benzyl-*N*-methylamine (1.33 mL, 10 mmol) and triethylamine (3.50 mL, 25 mmol) in toluene (70 mL) was added the appropriated aryldichlorophosphine (5 mmol) at -80 ºC. The reaction mixture was stirring for 30 min allowing reaching the temperature. Then, the toluene was distilled and THF (20 mL) was added. Oxidation of the arylphosphonamine was performed by addition of 30% v/v (0.51 mL, 5 mmol) hydrogen peroxide. Once the oxidation was complete (30 min), the reaction was poured into ice water and extracted with ethyl acetate (3 x 15 mL) and washed with 1N NaOH (2 x 15 mL) and water (1 x 15 mL). The organic layers were dried over $Na_2SO_4$ and concentrated in vacuo. Phenylphosphonamide **5** was precipitated from ether to give a white solid. The arylphosphonamides **11** and **13** were obtained as oils and were used without further purification. Phenylphosphonamide **5** has been previously described.[4]

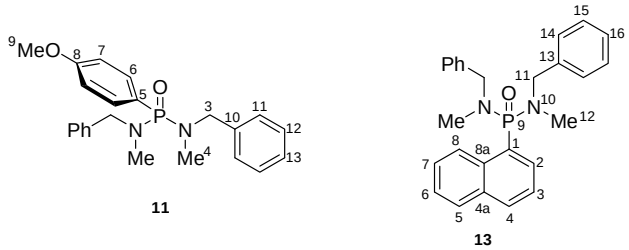


**Chart S1**. Scheme numbering used for the NMR assignments of arylphosphonamides **11** and **13**.

**Bis(*N*-benzyl-*N*-methyl)-*P*-(4-methoxiphenyl)phosphonamide (11).**

Crude reaction 95% (1.87 g). Oil. $^1$H NMR δ 2.57 (d, 6H, $^3J_{PH}$ 10.0 Hz, H-4), 3.83 (s, 3H, H-9), 4.18 (d, 2H, $^2J_{HH}$ 14.9 Hz, $^3J_{PH}$ 7.9 Hz, H-3), 4.25 (d, 2H, $^2J_{HH}$ 14.9 Hz, $^3J_{PH}$ 7.9 Hz, H-3'), 6.98 (dd, 2H, $^3J_{HH}$ 8.8 Hz, $^4J_{PH}$ 2.8 Hz, H-7), 7.21-7.32 (m, 10H, H-11, H-12, H-13), 7.83 (dd, 2H, $^3J_{HH}$ 8.8 Hz, $^3J_{PH}$ 11.4 Hz, H-6). $^{13}$C{$^1$H} NMR δ 33.27 (d, $^2J_{PC}$ 3.0 Hz, C-4), 52.41 (d, $^2J_{PC}$ 4.2 Hz, C-3), 55.22 (C-9), 114.04 (d, $^3J_{PC}$ 13.8 Hz, C-7), 122.09 (d, $^1J_{PC}$ 162.2 Hz, C-5), 127.08 (C-13), 128.12 (C-11), 128.38 (C-12), 134.02 (d, $^2J_{PC}$ 10.2 Hz, C-6), 138.06 (d, $^3J_{PC}$ 5.4 Hz, C-10), 162.12 (d, $^4J_{PC}$ 3.0 Hz, C-8). $^{31}$P{$^1$H} NMR δ 30.73. IR (KBr) 1175, 1116 cm$^{-1}$; MS (*m/z*) 395 (M+1, 100). Analysis: Calcd (%) for $C_{23}H_{27}N_2O_2P$ (394.17): C, 72.51; H, 6.91; N, 7.69. Found: C, 72.31; H, 6.95; N, 7.73.

**Bis(*N*-benzyl-*N*-methyl)-*P*-1-naphthylphosphonamide (13).**

Crude reaction 95% (1.97 g). Oil. $^1$H NMR δ 2.58 (d, 6H, $^3J_{PH}$ 9.5 Hz, H-12), 4.32 (dd, 2H, $^2J_{HH}$ 14.6 Hz $^3J_{PH}$ 7.8 Hz, H-11), 4.39 (dd, 2H, $^2J_{HH}$ 14.6 Hz $^3J_{PH}$ 7.9 Hz, H-11'), 7.24-7.37 (m, 6H, H-15, H-16), 7.34-7.47 (m, 4H, H-14), 7.48-7.55 (m, 2H, H-3, H-6), 7.61 (ddd, 1H, $^3J_{HH}$ 8.5 Hz, $^3J_{HH}$ 7.0 Hz, $^4J_{HH}$ 1.6 Hz, H-7), 7.80 (ddd, 1H, $^3J_{HH}$ 7.0 Hz, $^4J_{HH}$ 0.9 Hz, $^3J_{PH}$ 16.2 Hz, H-2), 7.86 (dt, 1H, $^3J_{HH}$ 8.1 Hz, $^4J_{HH}$ 1.6 Hz, $^5J_{PH}$ 1.6 Hz, H-5), 7.98 (d, 1H, $^3J_{HH}$ 8.3 Hz, H-4), 9.07 (d, $^3J_{HH}$ 8.5 Hz, H-

8). $^{13}C\{^1H\}$ NMR δ 34.04 (d, $^2J_{PC}$ 2.4 Hz, C-12), 52.74 (d, $^2J_{PC}$ 4.8 Hz, C-11), 124.40 (d, $^3J_{PC}$ 15.0 Hz, C-3), 126.41 (C-6), 127.27 (C-16), 127.36 (C-14), 127.40 (d, $^3J_{PC}$ 4.2 Hz, C-8), 127.94 (d, $^1J_{PC}$ 153.2 Hz, C-1), 128.37 (C-13), 128.61 (d, $^4J_{PC}$ 1.8 Hz, C-5), 128.76 (C-12), 131.95 (d, $^2J_{PC}$ 9.6 Hz, C-2), 132.82 (d, $^4J_{PC}$ 3.0 Hz, C-4), 133.95 (d, $^2J_{PC}$ 6.0 Hz, C-8a), 134.09 (d, $^3J_{PC}$ 5.4 Hz, C-4a), 137.85 (d, $^3J_{PC}$ 4.2 Hz, C-13). $^{31}P\{^1H\}$ NMR δ 31.69. IR (KBr) 1203 $cm^{-1}$; MS (*m/z*) 415 (M+1, 100). Analysis: Calcd (%) for $C_{26}H_{27}N_2OP$ (414.19): C, 75.34; H, 6.57; N, 6.76. Found: C, 75.32; H, 6.55; N, 6.74.

**General procedure for the dearomatizing anionic cyclization of phenylphosphonamides**.

To a solution of the appropriated arylphosphonamide **5**, **11** or **13** ($5.49x10^{-4}$ mol) and DMPU alternative (0.41 mL, $3.30x10^{-3}$ mol) in THF (20 mL) was added a solution of *s*-BuLi (1.06 mL, of a 1.3 M solution in cyclohexane, $1.37x10^{-3}$ mol) at –90 ºC. After the time of metalation (specified for each reaction in the main text) was added the corresponding electrophile (MeOH (1 mL), 2,6-di-*terc*-butil-4-metilfenol (DTBMP) (611.5 mg, $2.75x10^{-3}$ mol l) or aldehydes ($1.37x10^{-3}$ mol)). The reaction mixture was stirred at the same temperature of metalation for 30 min or 7 h (main text). Then the reaction mixture was poured into ice water and extracted with ethyl acetate (3x15 mL). The organic layers were dried over $Na_2SO_4$ and concentrated in vacuo. $^1H$, $^1H\{^{31}P\}$, and $^{31}P\{^1H\}$ NMR spectra of the crude reaction were measured in order to determine the regio- and stereoselectivity of the process. The reaction mixture was then purified by flash column chromatography using different mixtures of ethyl acetate:hexane as eluent.

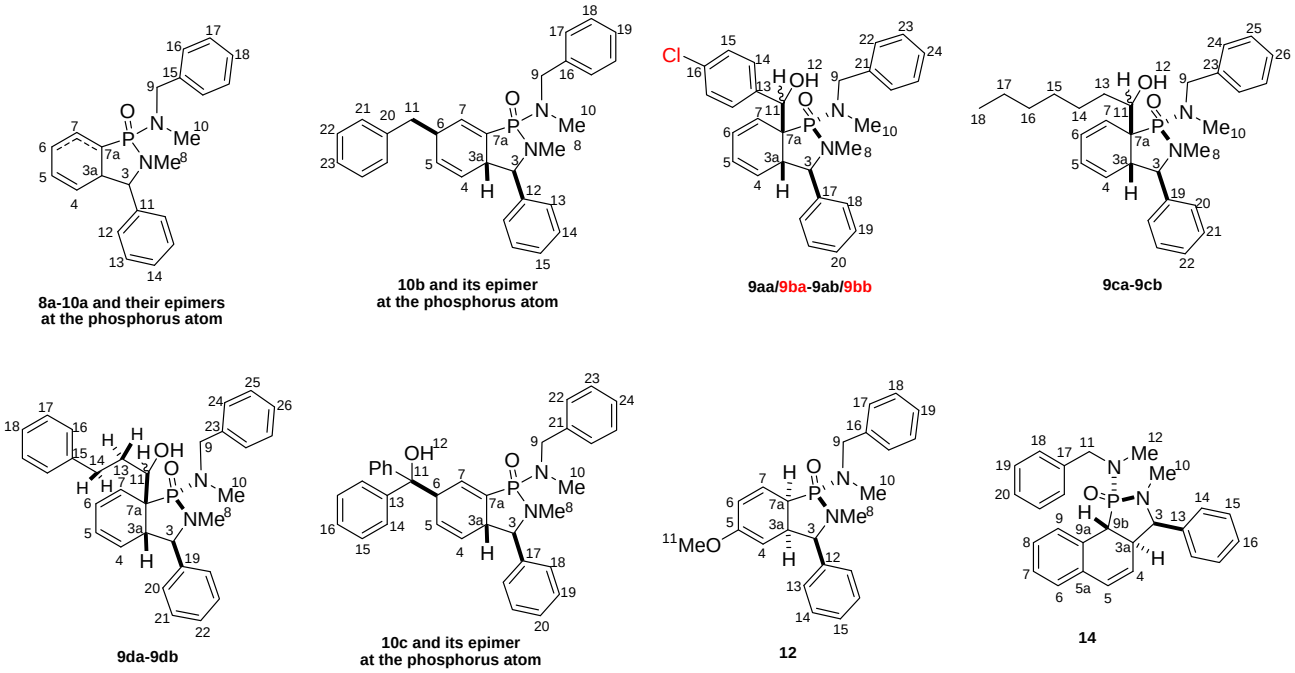


**Chart S2**. Scheme numbering used for the NMR assignments of benzazaphospholes **8-14**.

**(1*R*$_P$*,3*S**,3a*S**,7a*S**)-*N*-benzyl-3-phenyl-*N*,2-dimethyl-2,3,3a,7a-tetrahydro-1*H*-2,1-benzazaphosphol-1-amine 1-oxide (8a).**

Yield after flash chromatography (ethyl acetate/hexene, 3:1) 74% (148 mg). Oil. $^1$H NMR δ 2.36 (d, 3H, $^3J_{PH}$ 7.5 Hz, H-8), 2.54 (d, 3H, $^3J_{PH}$ 9.0 Hz, H-10), 3.05 (m, 1H, H-3a), 3.23 (ddt, 1H, $^3J_{HH}$ 11.7 Hz, $^{3,4}J_{HH}$ 2.4 Hz, $^2J_{PH}$ 23.6 Hz, H-7a), 4.00 (t, 1H, $^3J_{HH}$ 6.7 Hz, $^3J_{PH}$ 6.7 Hz, H-3), 4.33 (dd, 1H, $^2J_{HH}$ 14.4 Hz, $^3J_{PH}$ 8.7 Hz, H-9), 4.40 (dd, 1H, $^2J_{HH}$ 14.4 Hz, $^3J_{PH}$ 7.9 Hz, H-9'), 5.55 (dt, 1H, $^3J_{HH}$ 8.8 Hz, $^3J_{HH}$ 3.3 Hz, $^3J_{PH}$ 8.8 Hz, H-7), 5.64 (dd, 1H, $^3J_{HH}$ 8.4 Hz, $^3J_{HH}$ 5.0 Hz, H-4), 5.91-5.99 (m, 2H, H-5, H-6), 7.26-7.46 (m, 10H, ArH). $^{13}$C{$^1$H} NMR δ 28.40 (d, $^2J_{PC}$ 3.6 Hz, C-8), 33.81 (d, $^2J_{PC}$ 4.2 Hz, C-10), 36.31 (d, $^1J_{PC}$ 108.7 Hz, C-7a), 42.06 (d, $^2J_{PC}$ 3.6 Hz, C-3a), 53.41 (d, $^2J_{PC}$ 4.8 Hz, C-9), 70.60 (d, $^2J_{PC}$ 28.8 Hz, C-3), 120.35 (d, $^2J_{PC}$ 7.8 Hz, C-7), 123.59 (d, $^3J_{PC}$ 12.7 Hz, C-6), 123.98 (d, $^4J_{PC}$ 4.2 Hz, C-5), 126.51 (d, $^3J_{PC}$ 10.3 Hz, C-4), 127.10 (C12), 127.22 (C-18), 127.76 (C-14), 128.39 (C-16), 128.56 (C-13/C-16), 128.70 (C-13/C-16), 138.80 (d, $^3J_{PC}$ 3.0 HZ, C-15), 140.63 (d, $^3J_{PC}$ 3.0 Hz, C-11). $^{31}$P{$^1$H} NMR δ 48.03. IR (KBr) 1209, 1180 cm$^{-1}$; MS (*m/z*) 365 (M+1, 100). Analysis: Calcd (%) for $C_{22}H_{25}N_2OP$ (364.17): C, 72.51; H, 6.91; N, 7.69. Found: C, 72.31; H, 6.95; N, 7.73.

**(1*R*$_P$*,3*R**,3a*R**,7a*R**)-*N*-benzyl-3-phenyl-*N*,2-dimethyl-2,3,3a,7a-tetrahydro-1*H*-2,1-benzazaphosphol-1-amine 1-oxide (epimer of 8a at the phosphorus atom).**

Yield after flash chromatography (ethyl acetate/hexene, 3:1) 8% (16 mg). Oil. $^1$H NMR (500.13 MHz) δ 2.44 (d, 3H, $^3J_{PH}$ 8.6 Hz, H-8), 2.70 (m, 1H, H-3a), 2.83 (d, 3H, $^3J_{PH}$ 9.3 Hz, H-10), 2.84 (m, 1H, $^2J_{PH}$ 21.3 Hz, H-7a), 4.04 (dd, 1H, $^3J_{HH}$ 10.4 Hz, $^3J_{PH}$ 1.0 Hz, H-3), 4.44 (dd, 1H, $^2J_{HH}$ 14.8 Hz, $^3J_{PH}$ 8.4 Hz, H-9), 4.51 (dd, 1H, $^2J_{HH}$ 14.8 Hz, $^3J_{PH}$ 7.9 Hz, H-9'), 5.84 (ddddd, 1H, $^3J_{HH}$ 9.4 Hz, $^3J_{HH}$ 3.3 Hz, $^4J_{HH}$ 2.0 Hz, $^4J_{HH}$ 1.0 Hz, $^4J_{PH}$ 3.2 Hz, H-4), 6.00 (m, 1H, H-5), 6.13 (m, 1H, H-6), 6.18 (dddt, 1H, $^3J_{HH}$ 9.4 Hz, $^3J_{HH}$ 3.3 Hz, $^4J_{HH}$ 2.0 Hz, $^4J_{HH}$ 1.0 Hz, $^3J_{PH}$ 9.4 Hz, H-7), 7.45-7.28 (m, 10H, ArH). $^{13}$C{$^1$H} NMR (125.76 MHz) δ 28.59 (d, $^2J_{PC}$ 1.9 Hz, C-8), 34.33 (d, $^2J_{PC}$ 4.3 Hz, C-10), 40.41 (d, $^1J_{PC}$ 117.1 Hz, C-7a), 46.74 (d, $^2J_{PC}$ 2.9 Hz, C-3a), 53.36 (d, $^2J_{PC}$ 4.2 Hz, C-9), 66.42 (d, $^2J_{PC}$ 12.5 Hz, C-3), 122.92 (d, $^2J_{PC}$ 2.2 Hz, C-7), 126.56 (d, $^4J_{PC}$ 1.0 Hz, C-5), 127.07 (d, $^3J_{PC}$ 13.9 Hz, C-4), 127.29 (C14/C-17), 127.70 (C-6, C-12), 128.20 (C-16), 128.51 (C-14/C-17), 128.52 (C-13/C-16), 128.92 (C-13/C-16), 138.31 (d, $^3J_{PC}$ 8.2 HZ, C-15), 138.63 (d, $^3J_{PC}$ 3.8 Hz, C-11). $^{31}$P{$^1$H} NMR (202.46 MHz) δ 38.48. MS (*m/z*) 365 (M+1, 100). Analysis: Calcd (%) for $C_{22}H_{25}N_2OP$ (364.17): C, 72.51; H, 6.91; N, 7.69. Found: C, 72.46; H, 6.90; N, 7.65.

**(1*R*$_P$*,3*S**,3a*R**)-*N*-benzyl-3-phenyl-*N*,2-dimethyl-2,3,3a,6a-tetrahydro-1*H*-2,1-benzazaphosphol-1-amine 1-oxide (10a).**

Yield after flash chromatography (ethyl acetate/hexene, 4:1) 79% (158 mg). Oil. $^1$H NMR δ 2.29 (d, 3H, $^3J_{PH}$ 7.5 Hz, H-8), 2.40 (d, 3H, $^3J_{PH}$ 10.3 Hz, H-10), 2.75 (m, 2H, H-6), 3.18 (m, 1H, H-3a),

3.69 (d, 1H, $^{3}J_{HH}$ 8.9 Hz, H-3), 4.32 (d, 2H, $^{3}J_{PH}$ 8.4 Hz, H-9), 5.59 (dds, 1H, $^{3}J_{HH}$ 9.9 Hz, $^{3,4}J_{HH}$ 2.0 Hz, $^{4}J_{PH}$ 2.0 Hz, H-4), 5.75 (ddddt, 1H, $^{3}J_{HH}$ 9.9 Hz, $^{3}J_{HH}$ 4.0 Hz, $^{4}J_{HH}$ 2.9 Hz, $^{4}J_{HH}$ 1.3 Hz, $^{5}J_{PH}$ 1.3 Hz, H-5), 6.19 (dddt, 1H, $^{3}J_{HH}$ 4.2, Hz, $^{4}J_{HH}$ 2.9 Hz, $^{4}J_{HH}$ 1.3 Hz, $^{3}J_{PH}$ 18.2 Hz, H-7), 7.24-7.44 (m, 10H, ArH). $^{13}C\{^{1}H\}$ NMR δ 29.12 (d, $^{3}J_{PC}$ 14.4 Hz, C-6), 28.25 (d, $^{2}J_{PC}$ 4.2 Hz, C-8), 32.65 (d, $^{2}J_{PC}$ 6.7 Hz, C-10), 43.71 (d, $^{2}J_{PC}$ 19.8 Hz, C-3a), 52.92 (d, $^{2}J_{PC}$ 4.8 Hz, C-9), 70.57 (d, $^{2}J_{PC}$ 16.2 Hz, C-3), 123.34 (d, $^{3}J_{PC}$ 7.8 Hz, C-4), 124.85 (d, $^{4}J_{PC}$ 1.8 Hz, C-5), 127.25 (CHAr), 127.58 (CHAr), 128.04 (CHAr), 128.38 (CHAr), 128.72 (2CHAr), 129.89 (d, $^{2}J_{PC}$ 10.2 Hz, C-7), 129.90 (d, $^{1}J_{PC}$ 153.2 Hz, C-7a), 138.92 (d, $^{3}J_{PC}$ 3.6 HZ, C-15), 139.75 (d, $^{3}J_{PC}$ 3.0 Hz, C-11). $^{31}P\{^{1}H\}$ NMR δ 28.65. MS (*m/z*) 365 (M+1, 100). Analysis: Calcd (%) for $C_{22}H_{25}N_2OP$ (364.17): C, 72.51; H, 6.91; N, 7.69. Found: C, 72.58; H, 6.88; N, 7.67.

**(1*R*$_P$*,3*R**,3a*S**)-*N*-benzyl-3-phenyl-*N*,2-dimethyl-2,3,3a,6a-tetrahydro-1*H*-2,1-benzazaphosphol-1-amine 1-oxide (epimer of 10a at the phosphorus atom).**

Yield after flash chromatography (ethyl acetate/hexene, 4:1) 17% (34 mg). Oil. $^{1}H$ NMR δ 2.39 (d, 3H, $^{3}J_{PH}$ 8.5 Hz, H-8), 2.72 (d, 3H, $^{3}J_{PH}$ 9.9 Hz, H-10), 2.84 (m, 2H, H-6), 3.01 (m, 1H, H-3a), 3.86 (d, 1H, $^{3}J_{HH}$ 9.5 Hz, H-3), 4.30 (dd, 1H, $^{2}J_{HH}$ 15.0 Hz, $^{3}J_{PH}$ 8.9 Hz, H-9), 4.45 (dd, 1H, $^{2}J_{HH}$ 15.0 Hz, $^{3}J_{PH}$ 8.5 Hz, H-9'), 5.53 (m, 1H, H-4), 5.77 (ddddt, 1H, $^{3}J_{HH}$ 10.0 Hz, $^{3}J_{HH}$ 4.1 Hz, $^{4}J_{HH}$ 2.7 Hz, $^{4}J_{HH}$ 1.3 Hz, $^{5}J_{PH}$ 1.3 Hz, H-5), 6.70 (m, 1H, $^{3}J_{PH}$ 17.4 Hz, H-7), 7.26-7.42 (m, 10H, ArH). $^{13}C\{^{1}H\}$ NMR δ 27.67 (d, $^{3}J_{PC}$ 13.8 Hz, C-6), 28.20 (d, $^{2}J_{PC}$ 1.8 Hz, C-8), 33.44 (d, $^{2}J_{PC}$ 4.8 Hz, C-10), 46.09 (d, $^{2}J_{PC}$ 16.8 Hz, C-3a), 52.61 (d, $^{2}J_{PC}$ 4.8 Hz, C-9), 68.02 (d, $^{2}J_{PC}$ 16.8 Hz, C-3), 123.06 (d, $^{3}J_{PC}$ 7.2 Hz, C-4), 125.30 (C-5), 127.07 (CHAr), 127.62 (CHAr), 127.96 (CHAr), 128.16 (CHAr), 128.34 (CHAr), 128.74 (CHAr), 131.34 (d, $^{1}J_{PC}$ 146.7 Hz, C-7a), 133.46 (d, $^{2}J_{PC}$ 9.0 Hz, C-7), 138.70 (d, $^{3}J_{PC}$ 4.2 HZ, C-15), 139.16 (d, $^{3}J_{PC}$ 9.6 Hz, C-11). $^{31}P\{^{1}H\}$ NMR δ 29.97. MS (*m/z*) 365 (M+1, 100). Analysis: Calcd (%) for $C_{22}H_{25}N_2OP$ (364.17): C, 72.51; H, 6.91; N, 7.69. Found: C, 72.55; H, 6.90; N, 7.71.

**(1*R*$_P$*,3*S**,3a*R**,6*S**)-*N*,6-dibenzyl-3-phenyl-*N*,2-dimethyl-2,3,3a,6a-tetrahydro-1*H*-2,1-benzazaphosphol-1-amine 1-oxide (10b).**

Yield after flash chromatography (ethyl acetate/hexene, 2:1) 75% (187 mg). Oil. $^{1}H$ NMR δ 2.30 (d, 3H, $^{3}J_{PH}$ 7.6 Hz, H-8), 2.37 (d, 3H, $^{3}J_{PH}$ 10.4 Hz, H-10), 2.67 (d, 1H, $^{2}J_{HH}$ 6.7 Hz, H-11), 2.69 (d, 1H, $^{2}J_{HH}$ 6.7 Hz, H-11'), 3.08 (m, 1H, H-6), 3.16 (m, 1H, H-3a), 3.67 (d, $^{3}J_{HH}$ 8.5 Hz, 1H, H-3), 4.28 (dd, 1H, $^{2}J_{HH}$ 14.5 Hz, $^{3}J_{PH}$ 8.8 Hz, H-9), 4.36 (dd, 1H, $^{2}J_{HH}$ 14.5 Hz, $^{3}J_{PH}$ 7.9 Hz, H-9'), 5.64 (ddd, 1H, $^{3}J_{HH}$ 9.9 Hz, $^{4}J_{HH}$ 1.5 Hz, $^{4}J_{PH}$ 4.1 Hz, H-4), 5.72 (m, 1H, H-5), 6.18 (dddd, 1H, $^{3}J_{HH}$ 4.6 Hz, $^{4}J_{HH}$ 2.9 Hz, $^{4}J_{HH}$ 1.5 Hz, $^{3}J_{PH}$ 18.3 Hz, H-7), 7.18 (m, 2H, ArH), 7.30 (m, 7H, ArH), 7.41 (m, 6H, ArH). $^{13}C\{^{1}H\}$ NMR δ 28.31 (d, $^{2}J_{PC}$ 3.6 Hz, C-8), 32.58 (d, $^{2}J_{PC}$ 6.0 Hz, C-10), 39.26 (d, $^{3}J_{PC}$ 13.8 Hz, C-6), 42.00 (d, $^{4}J_{PC}$ 1.8 Hz, C-11), 44.08 (d, $^{2}J_{PC}$ 19.8 Hz, C-3a), 52.89 (d, $^{2}J_{PC}$ 4.8 Hz, C-9), 70.37 (d, $^{2}J_{PC}$ 16.2 Hz, C-3), 123.77 (d, $^{3}J_{PC}$ 8.4 Hz, C-4), 126.17, 127.22 (C-13), 127.59

(CHAr), 128.08 (CHAr), 128.29 (CHAr), 128.35 (CHAr), 128.69 (CHAr), 128.75 (CHAr), 129.13 (C-21), 129.49 (C-5), 130.40 (d, $^{1}J_{PC}$ 142.6 Hz, C-7a), 133.62 (d, $^{2}J_{PC}$ 9.0 Hz, C-7), 138.79 (C-20), 138.87 (d, $^{3}J_{PC}$ 3.6 Hz, C-16), 139.69 (d, $^{3}J_{PC}$ 4.8 Hz, C-12). $^{31}P\{^{1}H\}$ NMR δ 28.67. IR (KBr) 1261, 1017 cm$^{-1}$; MS (*m/z*) 455 (M+1, 100). Analysis: Calcd (%) for $C_{29}H_{31}N_2OP$ (454.22): C, 76.63; H, 6.87; N, 6.16. Found: C, 76.66; H, 6.90; N, 6.17.

**(1*R*$_P$*,3*R**,3a*S**,6*R**)-*N*,6-dibenzyl-3-phenyl-*N*,2-dimethyl-2,3,3a,6a-tetrahydro-1*H*-2,1-benzazaphosphol-1-amine 1-oxide (epimer of 10b at the phosphorus atom).**

Yield after flash chromatography (ethyl acetate/hexene, 2:1) 11% (27 mg). Oil. $^{1}H$ NMR δ 2.35 (d, 3H, $^{3}J_{PH}$ 8.5 Hz, H-8), 2.64 (m, 1H, H-3a), 2.65 (d, 3H, $^{3}J_{PH}$ 10.0 Hz, H-10), 2.76 (d, 2H, $^{3}J_{HH}$ 6.4 Hz, H-11), 3.19 (m, 1H, H-6), 3.76 (d, 1H, $^{3}J_{HH}$ 9.4 Hz, H-3), 4.20 (dd, 1H, $^{2}J_{HH}$ 15.0 Hz, $^{3}J_{PH}$ 9.4 Hz, H-9), 4.46 (dd, 1H, $^{2}J_{HH}$ 15.0 Hz, $^{3}J_{PH}$ 8.2 Hz, H-9'), 5.53 (ddd, 1H, $^{3}J_{HH}$ 10.1 Hz, $^{4}J_{HH}$ 2.3 Hz, $^{4}J_{PH}$ 4.1 Hz, H-4), 5.75 (ddddd, 1H, $^{3}J_{HH}$ 10.1 Hz, $^{3}J_{HH}$ 4.1 Hz, $^{4}J_{HH}$ 2.9 Hz, $^{4}J_{HH}$ 1.5 Hz, $^{5}J_{PH}$ 1.2 Hz, H-5), 6.65 (dddd, 1H, $^{3}J_{HH}$ 4.7 Hz, $^{4}J_{HH}$ 2.9 Hz, $^{4}J_{HH}$ 1.2 Hz, $^{3}J_{PH}$ 17.3 Hz, H-7), 7.06 (m, 2H, ArH, H-21), 7.19 (m, 2H, ArH), 7.23 (m, 3H, ArH), 7.36 (m, 8H, ArH). $^{13}C\{^{1}H\}$ NMR δ 28.13 (d, $^{2}J_{PC}$ 1.2 Hz, C-8), 33.41 (d, $^{2}J_{PC}$ 4.8 Hz, C-10), 39.52 (d, $^{3}J_{PC}$ 13.2 Hz, C-6), 41.11 (d, $^{4}J_{PC}$ 1.8 Hz, C-11), 46.35 (d, $^{2}J_{PC}$ 16.8 Hz, C-3a), 52.64 (d, $^{2}J_{PC}$ 5.4 Hz, C-9), 67.72 (d, $^{2}J_{PC}$ 16.2 Hz, C-3), 123.98 (d, $^{3}J_{PC}$ 7.2 Hz, C-4), 126.05 (CHAr), 127.15 (CHAr), 127.60 (CHAr), 127.99 (CHAr), 128.15 (CHAr), 128.41 (CHAr), 128.75 (CHAr), 129.37 (C-21), 129.65 (C-5), 132.24 (d, $^{1}J_{PC}$ 145.4 Hz, C-7a), 137.12 (d, $^{2}J_{PC}$ 7.8 Hz, C-7), 138.26 (C-20), 138.70 (d, $^{3}J_{PC}$ 3.6 Hz, C-16), 139.00 (d, $^{3}J_{PC}$ 9.6 Hz, C-12). $^{31}P\{^{1}H\}$ NMR δ 29.37. IR (KBr) 1098, 1075 cm$^{-1}$; MS (*m/z*) 455 (M+1, 100). Analysis: Calcd (%) for $C_{29}H_{31}N_2OP$ (454.22): C, 76.63; H, 6.87; N, 6.16. Found: C, 76.64; H, 6.89; N, 6.14.

**(1*R*$_p$*,3*S**,3a*R**,7a*R**,11*S**)-1-{1-[Benzyl(methyl)amino]-3-phenyl-2-methyl-1-oxido-2,3,3a,7a-tetrahydro-1*H*-2,1-benzazaphosphol-7a-yl}(phenyl)methanol (9aa).**

Yield after flash chromatography (ethyl acetate/hexene, 1:2) 47% (121 mg). Mp 123 ºC. $^{1}H$ NMR (55 ºC) δ 2.29 (d, 3H, $^{3}J_{PH}$ 7.2 Hz, H-8), 2.53 (d, 3H, $^{3}J_{PH}$ 8.9 Hz, H-10), 3.53 (m, 1H, H-3a), 3.63 (dd, 1H, $^{3}J_{HH}$ 8.9 Hz, $^{3}J_{PH}$ 1.6 Hz, H-3), 4.39 (dd, 1H, $^{2}J_{HH}$ 14.3 Hz, $^{3}J_{PH}$ 8.1 Hz, H-9), 4.50 (dd, 1H, $^{2}J_{HH}$ 14.4 Hz, $^{3}J_{PH}$ 9.8 Hz, H-9'), 4.95 (dd, 1H, $^{3}J_{HH}$ 1.3 Hz, $^{3}J_{PH}$ 6.5 Hz, H-11), 5.18-5.27 (m, 2H, H-4, H-5), 5.33 (t, 1H, $^{3}J_{HH}$ 9.8 Hz, $^{3}J_{PH}$ 9.8 Hz, H-7), 5.81 (m, 1H, H-6), 6.04 (m, 1H, H-12, OH), 7.04-7.16 (m, 3H, ArH), 7.22 (d, 2H, $^{3}J_{HH}$ 7.4 Hz, H-14), 7.32-7.45 (m, 8H, ArH), 7.52 (d, 2H, $^{3}J_{HH}$ 7.1 Hz, H-22). $^{13}C\{^{1}H\}$ NMR (55 ºC) δ 28.21 (d, $^{2}J_{PC}$ 3.5 Hz, C-8), 33.73 (d, $^{2}J_{PC}$ 3.6 Hz, C-10), 40.85 (d, $^{2}J_{PC}$ 6.9 Hz, C-3a), 49.91 (d, $^{1}J_{PC}$ 108.7 Hz, C-7a), 53.65 (d, $^{2}J_{PC}$ 4.4 Hz, C-9), 70.00 (d, $^{2}J_{PC}$ 29.4 Hz, C-3), 74.44 (d, $^{2}J_{PC}$ 3.5 Hz, C-11), 121.13 (d, $^{4}J_{PC}$ 3.5 Hz, C-5), 121.92 (d, $^{2}J_{PC}$ 7.2 Hz, C-7), 125.50 (d, $^{3}J_{PC}$ 10.7 Hz, C-6), 125.95 (CHAr), 126.94 (CHAr), 127.12 (d, $^{3}J_{PC}$ 12.2 Hz, C-4), 127.49 (CHAr), 127.56 (CHAr), 127.66 (CHAr), 127.96 (CHAr), 128.48 (CHAr), 128.63

(CHAr), 128.82 (CHAr), 138.52, (bs, C-21), 138.99 (d, $^3J_{PC}$ 13.1 Hz, C-13), 140.45 (d, $^3J_{PC}$ 6.0 Hz, C-17). $^{31}P\{^1H\}$ NMR (55 ºC) δ 51.69. IR (KBr) 3526, 3457, 1149 $cm^{-1}$; MS (*m/z*) 471 (M+1, 100). Analysis: Calcd (%) for $C_{29}H_{31}N_2O_2P$ (470.21): C, 74.02; H, 6.64; N, 5.95. Found: C, 74.12; H, 6.66; N, 5.91.

**(1*R*$_p$*,3*S**,3a*R**,7a*R**,11*R**)-1-{1-[Benzyl(methyl)amino]-3-phenyl-2-methyl-1-oxido-2,3,3a,7a-tetrahydro-1*H*-2,1-benzazaphosphol-7a-yl}(phenyl)methanol (9ab).**

Yield after flash chromatography (ethyl acetate/hexene, 1:2) 37% (95 mg). Mp 147 ºC. $^1H$ NMR (60 ºC) δ 2.25 (d, 3H, $^3J_{PH}$ 7.4 Hz, H-8), 2.34 (d, 3H, $^3J_{PH}$ 8.8 Hz, H-10), 3.55 (ddd, 1H, $^3J_{HH}$ 9.0 Hz, $^3J_{HH}$ 5.9 Hz, $^3J_{PH}$ 2.3 Hz, H-3a), 3.59 (dd, 1H, $^2J_{HH}$ 14.4 Hz, $^3J_{PH}$ 8.1 Hz, H-9), 3.78 (dd, 1H, $^3J_{HH}$ 9.0 Hz, $^3J_{PH}$ 2.9 Hz, H-3), 4.57 (dd, 1H, $^2J_{HH}$ 14.4 Hz, $^3J_{PH}$ 7.7 Hz, H-9'), 4.61 (dd, 1H, $^3J_{HH}$ 9.8 Hz, $^3J_{PH}$ 24.8 Hz, H-11), 5.36 (tq, 1H, $^3J_{HH}$ 9.8 Hz, $^4J_{HH}$ 1.1 Hz, $^3J_{PH}$ 9.8 Hz, H-7), 5.59 (dddt, 1H, $^3J_{HH}$ 9.3 Hz, $^3J_{HH}$ 5.9 Hz, $^4J_{HH}$ 1.1 Hz, $^4J_{PH}$ 3.0 Hz, H-4), 5.99 (dddq, 1H, $^3J_{HH}$ 9.3 Hz, $^3J_{HH}$ 5.3 Hz, $^4J_{HH}$ 1.1 Hz, $^5J_{PH}$ 1.1 Hz, H-5), 6.01 (bd, 1H,$^3J_{HH}$ 9.8 Hz, H-12), 6.15 (dddd, 1H, $^3J_{HH}$ 9.8 Hz, $^3J_{HH}$ 5.3 Hz, $^4J_{HH}$ 1.1 Hz, $^4J_{PH}$ 1.6 Hz, H-6), 7.20 (dd, 2H, $^3J_{HH}$ 7.8 Hz, $^4J_{HH}$ 1.9 Hz, H-22), 7.24-7.43 (m, 11H, ArH), 7.52 (dd, 2H, $^3J_{HH}$ 7.7 Hz, $^4J_{HH}$ 1.9 Hz, H-14). $^{13}C\{^1H\}$ NMR δ 28.41 (d, $^2J_{PC}$ 3.6 Hz, C-8), 33.50 (d, $^2J_{PC}$ 3.6 Hz, C-10), 44.90 (d, $^2J_{PC}$ 7.8 Hz, C-3a), 48.39 (d, $^1J_{PC}$ 113.5 Hz, C-7a), 52.80 (d, $^2J_{PC}$ 4.8 Hz, C-9), 67.65 (d, $^2J_{PC}$ 24.6 Hz, C-3), 73.78 (d, $^2J_{PC}$ 4.2 Hz, C-11), 123.52 (d, $^4J_{PC}$ 3.0 Hz, C-5), 123.66 (d, $^2J_{PC}$ 4.2 Hz, C-7), 124.74 (d, $^3J_{PC}$ 10.2 Hz, C-6), 125.65 (d, $^3J_{PC}$ 12.0 Hz, C-4), 126.89-128.63 (9CHAr), 138.01, (sa, C-13), 139.86 (d, $^3J_{PC}$ 4.2 Hz, C-17), 141.63 (d, $^3J_{PC}$ 3.0 Hz, C-21). $^{31}P\{^1H\}$ NMR (60 ºC) δ 49.66. IR (KBr) 3263, 1178 $cm^{-1}$; MS (*m/z*) 471 (M+1, 100). Analysis: Calcd (%) for $C_{29}H_{31}N_2O_2P$ (470.21): C, 74.02; H, 6.64; N, 5.95. Found: C, 74.06; H, 6.58; N, 5.97.

**(1*R*$_p$*,3*S**,3a*R**,7a*R**,11*S**)-1-{1-[Benzyl(methyl)amino]-3-phenyl-2-methyl-1-oxido-2,3,3a,7a-tetrahydro-1*H*-2,1-benzazaphosphol-7a-yl}(*p*-chlorophenyl)methanol (9ba).**

Yield after flash chromatography (ethyl acetate/hexene, 1:3) 44% (120 mg). Oil. $^1H$ NMR (60 ºC) δ 2.29 (d, 3H, $^3J_{PH}$ 7.5 Hz, H-8), 2.54 (d, 3H, $^3J_{PH}$ 9.0 Hz, H-10), 3.47 (ddt, 1H, $^3J_{HH}$ 8.9 Hz, $^3J_{HH}$ 5.6 Hz, $^4J_{HH}$ 1.3 Hz, $^3J_{PH}$ 5.6 Hz, H-3a), 3.63 (dd, 1H, $^3J_{HH}$ 8.9 Hz, $^3J_{PH}$ 1.9 Hz, H-3), 4.39 (dd, 1H, $^2J_{HH}$ 14.3 Hz, $^3J_{PH}$ 8.1 Hz, 1H, H-9), 4.49 (dd, 1H, $^2J_{HH}$ 14.3 Hz, $^3J_{PH}$ 10.1 Hz, 1H, H-9'), 4.90 (dd, 1H, $^3J_{HH}$ 2.0 Hz, $^3J_{PH}$ 6.5 Hz, H-11), 5.22 (ddq, 1H, $^3J_{HH}$ 9.5 Hz, $^3J_{HH}$ 5.6 Hz, $^4J_{HH}$ 1.1 Hz, $^4J_{PH}$ 1.1 Hz, H-4), 5.26-5.36 (m, 2H, H-5, H-7), 5.84 (dddd, 1H, $^3J_{HH}$ 9.5 Hz, $^3J_{HH}$ 5.4 Hz, $^4J_{HH}$ 1.1 Hz, $^4J_{PH}$ 1.6 Hz, H-6), 6.09 (dd, $^3J_{HH}$ 2.0 Hz, $^4J_{PH}$ 0.6 Hz, 1H, H-12, OH), 7.05 (m, 2H, $^3J_{HH}$ 8.5 Hz, H-15), 7.17 (m, 2H, $^3J_{HH}$ 8.5 Hz, H-14), 7.15-7.46 (m, 8H, ArH), 7.51 (m, 2H, H-22). $^{13}C\{^1H\}$ NMR (60 ºC) δ 28.34 (d, $^2J_{PC}$ 3.6 Hz, C-8), 33.93 (d, $^2J_{PC}$ 3.6 Hz, C-10), 40.93 (d, $^2J_{PC}$ 7.2 Hz, C-3a), 49.92 (d, $^1J_{PC}$ 108.7 Hz, C-7a), 53.82 (d, $^2J_{PC}$ 4.2 Hz, C-9), 69.89 (d, $^2J_{PC}$ 28.8 Hz, C-3), 74.00 (d, $^2J_{PC}$ 3.0, C-11), 121.62 (d, $^4J_{PC}$ 3.6 Hz, C-5), 121.92 (d, $^2J_{PC}$ 7.2 Hz, C-7), 125.94 (d, $^3J_{PC}$ 10.8 Hz, C-6),

126.29 (C-15), 127.29 (d, $^3J_{PC}$ 12.0 Hz, C-4), 127.70 (CHAr), 127.78 (C-18), 128.19 (CHAr), 128.66 (CHAr), 128.83 (CHAr), 128.93 (C-14), 128.97 (C-22), 132.92 (C-16), 137.77 (d, $^3J_{PC}$ 13.2 Hz, C-13), 138.63 (d, $^3J_{PC}$ 1.8 Hz, C-21), 140.44 (d, $^3J_{PC}$ 6.0 Hz, C-17). $^{31}P\{^1H\}$ NMR (60 ºC) δ 51.89. IR (KBr) 3225, 1166 cm$^{-1}$; MS (*m/z*) 505 (M+1, 100). Analysis: Calcd (%) for $C_{29}H_{30}N_2O_2PCl$ (504.17): C, 68.97; H, 5.99; N, 5.55. Found: C, 68.95; H, 6.00; N, 5.52.

**(1*R*$_p$*,3*S**,3a*R**,7a*R**,11*R**)-1-{1-[Benzyl(methyl)amino]-3-phenyl-2-methyl-1-oxido-2,3,3a,7a-tetrahydro-1*H*-2,1-benzazaphosphol-7a-yl}(*p*-chlorophenyl)methanol (9bb).**

Yield after flash chromatography (ethyl acetate/hexene, 1:3) 38% (106 mg). Mp 205 ºC. $^1H$ NMR (55 ºC) δ 2.25 (d, 3H, $^3J_{PH}$ 7.6 Hz, H-8),2.36 (d, 3H, $^3J_{PH}$ 9.1 Hz, H-10), 3.50 (ddd, 1H, $^3J_{HH}$ 8.5 Hz, $^3J_{HH}$ 5.9 Hz, $^3J_{PH}$ 2.4 Hz, H-3a), 3.68 (dd, 1H, $^2J_{HH}$ 14.6 Hz, $^3J_{PH}$ 8.2 Hz, H-9), 3.78 (dd, 1H, $^3J_{HH}$ 8.9 Hz, $^3J_{PH}$ 2.9 Hz, H-3), 4.53 (dd, 1H, $^2J_{HH}$ 14.6 Hz, $^3J_{PH}$ 7.8 Hz, H-9'), 4.59 (dd, 1H, $^3J_{HH}$ 9.7 Hz, $^3J_{PH}$ 23.9 Hz, H-11), 5.36 (tq, 1H, $^3J_{HH}$ 9.5 Hz, $^4J_{HH}$ 0.9 Hz, $^3J_{PH}$ 9.5 Hz, H-7), 5.59 (dddt, 1H, $^3J_{HH}$ 9.5 Hz, $^3J_{HH}$ 6.0 Hz, $^4J_{HH}$ 0.9 Hz, $^4J_{PH}$ 2.9 Hz, 1H, H-4), 5.98 (ddq, 1H, $^3J_{HH}$ 9.5 Hz, $^3J_{HH}$ 5.5 Hz, $^4J_{HH}$ 0.9 Hz, $^5J_{PH}$ 0.9 Hz, H-5), 6.02 (dd, 1H, $^3J_{HH}$ 9.7 Hz, $^4J_{PH}$ 0.9 Hz, H-12, OH), 6.15 (dddd, 1H, $^3J_{HH}$ 9.5 Hz, $^3J_{HH}$ 5.5 Hz, $^4J_{HH}$ 0.9 Hz, $^4J_{PH}$ 1.7 Hz, H-6), 7.20 (m, 2H, H-22), 7.25-7.33 (m, 5H, ArH), 7.33-7.48 (m, 7H, ArH). $^{13}C\{^1H\}$ NMR (55 ºC) δ 28.27 (d, $^2J_{PC}$ 3.6 Hz, C-8), 33.45 (d, $^2J_{PC}$ 3.0 Hz, C-10), 45.20 (d, $^2J_{PC}$ 7.2 Hz, C-3a), 48.53 (d, $^1J_{PC}$ 112.3 Hz, C-7a), 59.95 (d, $^2J_{PC}$ 4.8 Hz, C-9), 68.10, (d, $^2J_{PC}$ 25.8 Hz, C-3), 74.06 (d, $^2J_{PC}$ 4.2, C-11), 123.30 (d, $^4J_{PC}$ 3.0 Hz, C-5), 123.39 (d, $^2J_{PC}$ 4.8 Hz, C-7), 124.83 (d, $^3J_{PC}$ 10.2 Hz, C-6), 125.75 (d, $^3J_{PC}$ 12.0 Hz, C-4), 127.24-128.65 (7 CHAr), 129.69 (C-14), 133.10 (C-16), 137.86 (d, $^3J_{PC}$ 3.6 Hz, C-21), 139.89 (d, $^3J_{PC}$ 4.2 Hz, C-17), 140.20 (d, $^3J_{PC}$ 4.2 Hz, C-13). $^{31}P\{^1H\}$ NMR (55 ºC) δ 50.08. IR (KBr) 3270, 1181 cm$^{-1}$; MS (*m/z*) 505 (M+1, 100). Analysis: Calcd (%) for $C_{29}H_{30}N_2O_2PCl$ (504.17): C, 68.97; H, 5.99; N, 5.55. Found: C, 68.99; H, 6.05; N, 5.62.

**(1*R*$_p$*,3*S**,3a*R**,7a*R**,11*S**)-1-{1-[Benzyl(methyl)amino]-3-phenyl-2-methyl-1-oxido-2,3,3a,7a-tetrahydro-1*H*-2,1-benzazaphosphol-7a-yl}heptanol (9ca).**

Yield after flash chromatography (ethyl acetate/hexene, 1:3) 28% (73 mg). Oil. $^1H$ NMR (60 ºC) δ 0.90 (t, 3H, $^3J_{HH}$ 6.7 Hz, H-18), 1.18-1.40 (m, 8H), 1.49-1.62 (m, 2H), 2.26 (d, 3H, $^3J_{PH}$ 7.3 Hz, H-8), 2.49 (d, 3H, $^3J_{PH}$ 8.9 Hz, H-10), 3.36 (ddd, 1H, $^3J_{HH}$ 8.7 Hz, $^3J_{HH}$ 5.8 Hz, $^3J_{PH}$ 2.6 Hz, H-3a), 3.69 (dd, 1H, $^3J_{HH}$ 8.9 Hz, $^3J_{PH}$ 1.9 Hz, H-3), 3.94 (m, 1H, H-11), 4.26 (dd, 1H, $^2J_{HH}$ 14.4 Hz, $^3J_{PH}$ 8.0, H-9), 4.49 (dd, 1H, $^2J_{HH}$ 14.4 Hz, $^3J_{PH}$ 8.9 Hz, H-9'), 5.26 (dd, 1H, $^3J_{HH}$ 2.0 Hz, $^4J_{PH}$ 1.2 Hz, H-12, OH), 5.35 (ddd, 1H, $^3J_{HH}$ 9.8 Hz, $^4J_{HH}$ 0.9 Hz, $^3J_{PH}$ 9.8 Hz, H-7), 5.69 (dddt, 1H, $^3J_{HH}$ 9.5 Hz, $^3J_{HH}$ 5.8, $^4J_{HH}$ 1.2 Hz, $^4J_{PH}$ 2.5 Hz, H-4), 5.92 (ddc, 1H, $^3J_{HH}$ 9.5 Hz, $^3J_{HH}$ 5.5 Hz, $^4J_{HH}$ 0.9 Hz, $^5J_{PH}$ 0.9 Hz, H-5), 6.08 (dddd, 1H, $^3J_{HH}$ 9.5 Hz, $^3J_{HH}$ 5.5 Hz, $^4J_{HH}$ 0.9 Hz, $^4J_{PH}$ 2.9 Hz, H-6), 7.28-7.40 (m, 8H, ArH), 7.46 (m, 2H, H-24). $^{13}C\{^1H\}$ NMR (60 ºC) δ 13.75 (C-18), 22.45 (C-17), 26.94 (d, $^4J_{PC}$ 0.8 Hz, C-14), 28.07 (d, $^2J_{PC}$ 3.7 Hz, C-8), 29.04 (C15), 29.62 (d, $^3J_{PC}$ 11.2 Hz, C-13), 31.74

(C-16), 33.53 (d, $^2J_{PC}$ 3.3 Hz, C-10), 41.12 (d, $^2J_{PC}$ 6.6 Hz, C-3a), 48.91 (d, $^1J_{PC}$ 108.8 Hz, C-7a), 53.62 (d, $^2J_{PC}$ 4.1 Hz, C-9), 70.62 (d, $^2J_{PC}$ 30.2 Hz, C-3), 73.67 (d, $^2J_{PC}$ 5.0 Hz, C-11), 122.39 (d, $^4J_{PC}$ 3.7 Hz, C-5), 123.11 (d, $^2J_{PC}$ 7.4 Hz, C-7), 124.67 (d, $^3J_{PC}$ 11.2 Hz, C-6), 127.32 (CHAr), 127.64 (d, $^3J_{PC}$ 12.0 Hz, C-4), 127.67 (CHAr), 128.35 (CHAr), 128,58 (CHAr), 128.69 (CHAr), 138.56 (d, $^3J_{PC}$ 2.1 Hz, C-23), 140. 64 (d, $^3J_{PC}$ 6.2 Hz, C-19). $^{31}P\{^1H\}$ NMR (60 ºC) δ 53.07. IR (KBr) 3250, 1168 cm$^{-1}$; MS (*m/z*) 479 (M+1, 100). Analysis: Calcd (%) for $C_{29}H_{39}N_2O_2P$ (478.27): C, 72.78; H, 8.21; N, 5.85. Found: C, 72.74; H, 8.25; N, 5.82.

**(1*R*$_p$*,3*S**,3a*R**,7a*R**,11*R**)-1-{1-[Benzyl(methyl)amino]-3-phenyl-2-methyl-1-oxido-2,3,3a,7a-tetrahydro-1*H*-2,1-benzazaphosphol-7a-yl}heptanol (9cb).**

Yield after flash chromatography (ethyl acetate/hexene, 1:3) 56% (147 mg). Oil. $^1H$ NMR (45 ºC) δ 0.89 (m, 3H, H-18), 1.32 (m, 8H), 1.58-1.86 (m, 2H, H-13), 2.24 (d, 3H, $^3J_{PH}$ 7.4 Hz, H-8), 2.50 (d, 3H, $^3J_{PH}$ 8.9 Hz, H-10), 3.29 (ddd, 1H, $^3J_{HH}$ 8.9 Hz, $^3J_{HH}$ 5.8 Hz, $^3J_{PH}$ 2.3 Hz, H-3a), 3.43 (dt, 1H, $^3J_{HH}$ 9.6 Hz, $^3J_{PH}$ 23.4 Hz, H-11), 3.76 (dd, 1H, $^3J_{HH}$ 8.9 Hz, $^3J_{PH}$ 2.4 Hz, H-3), 3.98 (dd, 1H, $^2J_{HH}$ 14.4 Hz, $^3J_{PH}$ 8.3, H-9), 4.60 (d, 1H, $^3J_{HH}$ 9.6 Hz, H-12, OH), 4.75 (dd, 1H, $^2J_{HH}$ 14.4 Hz, $^3J_{PH}$ 7.3 Hz, H-9'), 5.58 (ddc, 1H, $^3J_{HH}$ 9.7 Hz, $^3J_{HH}$ 5.9 Hz, $^4J_{HH}$ 0.8 Hz, $^4J_{PH}$ 2.8 Hz, H-4), 5.70 (tq, 1H, $^3J_{HH}$ 9.7 Hz, $^4J_{HH}$ 0.8 Hz, $^3J_{PH}$ 9.7 Hz, H-7), 5.99 (ddc, 1H, $^3J_{HH}$ 9.7 Hz, $^3J_{HH}$ 5.4, $^4J_{HH}$ 0.8 Hz, $^5J_{PH}$ 0.8 Hz, H-5), 6.14 (ddc, 1H, $^3J_{HH}$ 9.7 Hz, $^3J_{HH}$ 5.4 Hz, $^4J_{HH}$ 0.8 Hz, $^4J_{PH}$ 0.8 Hz, H-6), 7.25-7.47 (m, 10H, ArH). $^{13}C\{^1H\}$ NMR (45 ºC) δ 13.87 (C-18), 22.47 (C-17), 26.69 (C-14), 28.21 (d, $^2J_{PC}$ 3.4 Hz, C-8), 29.12 (C15), 31.76 (C-16), 33.10 (d, $^3J_{PC}$ 4.7 Hz, C-13), 33.62 (d, $^2J_{PC}$ 3.5 Hz, C-10), 44.54 (d, $^2J_{PC}$ 7.1 Hz, C-3a), 48.06 (d, $^1J_{PC}$ 111.7 Hz, C-7a), 53.19 (d, $^2J_{PC}$ 4.8 Hz, C-9), 68.40 (d, $^2J_{PC}$ 26.8 Hz, C-3), 73.77 (d, $^2J_{PC}$ 4.7 Hz, C-11), 123.07 (d, $^4J_{PC}$ 3.3 Hz, C-5), 123.51 (d, $^2J_{PC}$ 5.0 Hz, C-7), 124.34 (d, $^3J_{PC}$ 10.8 Hz, C-6), 125.68 (d, $^3J_{PC}$ 12.0 Hz, C-4), 127.25 (CHAr), 127.64 (C-20), 127.90 (CHAr), 128.34 (CHAr), 128.55 (C-24), 128.59 (CHAr), 138.32 (d, $^3J_{PC}$ 2.7 Hz, C-23), 140.18 (d, $^3J_{PC}$ 5.2 Hz, C-19). $^{31}P\{^1H\}$ NMR (45 ºC) δ 51.34. IR (KBr) 3312, 1184, 1006 cm$^{-1}$; MS (*m/z*) 479 (M+1, 100). Analysis: Calcd (%) for $C_{29}H_{39}N_2O_2P$ (478.27): C, 72.78; H, 8.21; N, 5.85. Found: C, 72.80; H, 8.23; N, 5.88.

**(1*R*$_p$*,3*S**,3a*R**,7a*R**,11*S**)-1-{1-[Benzyl(methyl)amino]-3-phenyl-2-methyl-1-oxido-2,3,3a,7a-tetrahydro-1*H*-2,1-benzazaphosphol-7a-yl}-3-phenylpropanol (9da).**

Yield after flash chromatography (ethyl acetate/hexene, 1:3) 29% (79 mg). Oil. $^1H$ NMR (50 ºC) δ 1.60 (m, 1H, $H_R$-13), 1.90 (m, 1H, $H_S$-13), 2.27 (d, 3H, $^3J_{PH}$ 7.4 Hz, H-8), 2.46 (d, 3H, $^3J_{PH}$ 8.9 Hz, H-10), 2.61(ddd, 1H, $^2J_{HH}$ 14.0 Hz, $^3J_{HH}$ 9.2 Hz, $^3J_{HH}$ 7.4 Hz, $H_R$-14), 2.92 (ddd, 1H, $^2J_{HH}$ 14.0 Hz, $^3J_{HH}$ 9.4 Hz, $^3J_{HH}$ 4.7 Hz, $H_S$-14), 3.39 (ddd, 1H, $^3J_{HH}$ 8.9 Hz, $^3J_{HH}$ 5.9 Hz, $^3J_{PH}$ 2.4 Hz, H-3a), 3.69 (dd, 1H, $^3J_{HH}$ 8.9 Hz, $^3J_{PH}$ 2.0 Hz, H-3), 3.98 (ddt, 1H, $^3J_{HH}$ 10.6 Hz, $^3J_{HH}$ 2.0 Hz, $^3J_{PH}$ 2.0 Hz, H-11), 4.28 (dd, 1H, $^2J_{HH}$ 14.4 Hz, $^3J_{PH}$ 8.0 Hz, H-9), 4.43 (dd, 1H, $^2J_{HH}$ 14.4 Hz, $^3J_{PH}$ 8.9 Hz, H-9'), 5.26 (tq, 1H, $^3J_{HH}$ 9.7 Hz, $^3J_{PH}$ 9.7, $^4J_{HH}$ 1.1 Hz, H-7), 5.46 (dt, 1H, $^3J_{HH}$ 2.0 Hz, $^4J_{PH}$ 0.9 Hz, H-

12, OH), 5.68 (dddt, 1H, $^3J_{HH}$ 9.5 Hz, $^3J_{HH}$ 5.9 Hz, $^4J_{HH}$ 1.1 Hz, $^4J_{PH}$ 2.7 Hz, H-4), 5.91 (ddq, 1H, $^3J_{HH}$ 9.5 Hz, $^3J_{HH}$ 5.5 Hz, $^4J_{HH}$ 0.9 Hz, $^5J_{PH}$ 0.9 Hz, H-5), 6.06 (dddd, 1H, $^3J_{HH}$ 9.5 Hz, $^3J_{HH}$ 5.5 Hz, $^4J_{HH}$ 0.9 Hz, $^4J_{PH}$ 2.9 Hz, H-6), 7.19 (m, 2H, H-16), 7.24-7.44 (m, 13H, ArH). $^{13}C\{^1H\}$ NMR (50 ºC) δ 28.25 (d, $^2J_{PC}$ 3.6 Hz, C-8), 31.28 (d, $^3J_{PC}$ 11.4 Hz, C-13), 33.07 (d, $^4J_{PC}$ 1.2 Hz, C-14), 33.58 (d, $^2J_{PC}$ 3.6 Hz, C-10), 41.14 (d, $^2J_{PC}$ 6.6 Hz, C-3a), 48.81 (d, $^1J_{PC}$ 109.9 Hz, C-7a), 53.67 (d, $^2J_{PC}$ 4.2 Hz, C-9), 70.59 (d, $^2J_{PC}$ 30.0 Hz, C-3), 72.79 (d, $^2J_{PC}$ 4.2 Hz, C-11), 122.71 (d, $^4J_{PC}$ 3.6 Hz, C-5), 122.90 (d, $^2J_{PC}$ 7.2 Hz, C-7), 125.05 (d, $^3J_{PC}$ 10.8 Hz), 125.50 (C-18), 127.47 (CHAr), 127.71 (d, $^3J_{PC}$ 12.0 Hz, C-4), 127.77 (C-20), 128.10 (CHAr), 128.18 (CHAr), 128.52 (CHAr), 128.64 (C-16), 128.75 (CHAr), 128.82 (C-24), 138.52 (d, $^3J_{PC}$ 2.4 Hz, C-23), 140.65 (d, $^3J_{PC}$ 6.0 Hz, C-19), 142.61 (C-15). $^{31}P\{^1H\}$ NMR (50 ºC) δ 52.68. IR (KBr) 3344, 1179 $cm^{-1}$; MS (*m/z*) 499 (M+1, 100). Analysis: Calcd (%) for $C_{31}H_{35}N_2O_2P$ (498.24): C, 74.68; H, 7.08; N, 5.62. Found: C, 74.70; H, 7.05; N, 5.58.

**(1*R*$_p$*,3*S**,3a*R**,7a*R**,11*R**)-1-{1-[Benzyl(methyl)amino]-3-phenyl-2-methyl-1-oxido-2,3,3a,7a-tetrahydro-1*H*-2,1-benzazaphosphol-7a-yl}-3-phenylpropanol (9db).**

Yield after flash chromatography (ethyl acetate/hexene, 1:3) 59% (161 mg). Oil. $^1H$ NMR (50 ºC) δ 1.97 (m, 1H, $H_R$-13); 2.16 (m, 1H, $H_S$-13), 2.25 (d, 3H, $^3J_{PH}$ 7.4 Hz, H-8), 2.50 (d, 3H, $^3J_{PH}$ 9.0 Hz, H-10), 2.66 (ddd, 1H, $^2J_{HH}$ 13.8 Hz, $^3J_{HH}$ 9.7 Hz, $^3J_{HH}$ 6.7 Hz, $H_R$-14), 3.08 (ddd, 1H, $^2J_{HH}$ 13.8 Hz, $^3J_{HH}$ 10.0 Hz, $^3J_{HH}$ 4.8 Hz, $H_S$-14), 3.27 (ddd, 1H, $^3J_{HH}$ 8.8 Hz, $^3J_{HH}$ 5.9 Hz, $^3J_{PH}$ 2.6 Hz, H-3a), 3.52 (dddd, 1H, $^3J_{HH}$ 11.4 Hz, $^3J_{HH}$ 9.4 Hz, $^3J_{HH}$ 2.4 Hz, $^3J_{PH}$ 22.6 Hz, H-11), 3.76 (dd, 1H, $^3J_{HH}$ 8.8 Hz, $^3J_{PH}$ 2.4 Hz, H-3), 3.98 (dd, 1H, $^2J_{HH}$ 14.4 Hz, $^3J_{PH}$ 8.4 Hz, H-9), 4.74 (dd, 1H, $^2J_{HH}$ 14.4 Hz, $^3J_{PH}$ 7.4 Hz, H-9'), 4.82 (dd, 1H, $^3J_{HH}$ 9.4 Hz, $^4J_{PH}$ 0.9 Hz, H-12, OH), 5.58 (dddt, 1H, $^3J_{HH}$ 9.3 Hz, $^3J_{HH}$ 5.9 Hz, $^4J_{HH}$ 1.0 Hz, $^4J_{PH}$ 2.8 Hz, H-4), 5.71 (tq, 1H, $^3J_{HH}$ 9.8 Hz, $^4J_{HH}$ 1.0 Hz, $^3J_{PH}$ 9.8 Hz, H-7), 5.98 (ddq, 1H, $^3J_{HH}$ 9.3 Hz, $^3J_{HH}$ 5.4 Hz, $^4J_{HH}$ 1.0 Hz, $^5J_{PH}$ 1.0 Hz Hz, H-5), 6.13 (dddd, 1H, $^3J_{HH}$ 9.8 Hz, $^3J_{HH}$ 5.4 Hz, $^4J_{HH}$ 1.0 Hz, $^4J_{PH}$ 1.7 Hz, 1H, H-6), 7.14-7.40 (m, 13H, ArH), 7.45 (m, 2H, H-24). $^{13}C\{^1H\}$ NMR (50 ºC) δ 28.27 (d, $^2J_{PC}$ 3.6 Hz, C-8), 33.08 (C-14), 33.64 (d, $^2J_{PC}$ 3.6 Hz, C-10), 34.93 (d, $^3J_{PC}$ 4.8 Hz, C-13), 44.34 (d, $^2J_{PC}$ 7.2 Hz, C-3a), 47.99 (d, $^1J_{PC}$ 111.7 Hz, C-7a), 53.26 (d, $^2J_{PC}$ 4.8 Hz, C-9), 68.57 (d, $^2J_{PC}$ 226.4 Hz, C-3), 7359 (d, $^2J_{PC}$ 4.8 Hz, C-11), 123.44 (d, $^4J_{PC}$ 3.6 Hz, C-5), 123.14 (d, $^2J_{PC}$ 4.8 Hz, C-7), 124.57 (d, $^3J_{PC}$ 10.8 Hz, C-6), 125.53 (C-18), 125.68 (d, $^3J_{PC}$ 12.0 Hz, C-4), 127.33 (C-26), 127.69 (C-20), 128.01 (C-22), 128.22 (C-16), 128.42 (C-17/C-25), 128.46 (C-17/C-25), 128.65 (C-21/C-24), 128.70 (C-21/C-24), 138.30 (d, $^3J_{PC}$3.0 Hz, C-23), 140.18 (d, $^3J_{PC}$ 5.4 Hz, C-19), 142.57 (C-15). $^{31}P\{^1H\}$ NMR (50 ºC) δ 51.33. IR (KBr) 3360, 1180, 1164 $cm^{-1}$; MS (*m/z*) 499 (M+1, 100). Analysis: Calcd (%) for $C_{31}H_{35}N_2O_2P$ (498.24): C, 74.68; H, 7.08; N, 5.62. Found: C, 74.65; H, 7.12; N, 5.60.

**(1$R_p$*,3*S**,3a*R**,6*S**)-1-{1-[Benzyl(methyl)amino]-3-phenyl-2-methyl-1-oxido-2,3,3a,6-tetrahydro-1*H*-2,1-benzazaphosphol-6-yl}(diphenyl)methanol (10c).**

Yield after flash chromatography (ethyl acetate/hexene, 4:1) 60% (180 mg). Oil. $^1$H NMR δ 2.31 (d, 3H, $^3J_{PH}$ 7.5 Hz, H-8), 2.36 (d, 3H, $^3J_{PH}$ 10.6 Hz, H-10), 3.05 (bs, 1H, H-12, OH), 3.29 (m, 1H, H-3a), 3.67(dd, 1H, $^3J_{HH}$ 8.9 Hz, $^3J_{PH}$ 1.0 Hz, H-3), 4.08 (dd, 1H, $^2J_{HH}$ 14.3 Hz, $^3J_{PH}$ 9.5 Hz, H-9), 4.21 (m, 1H, H-6), 4.43 (dd, 1H, $^2J_{HH}$ 14.3 Hz, $^3J_{PH}$ 7.8 Hz, H-9'), 5.47 (ddddd, 1H, $^3J_{HH}$ 9.9 Hz, $^3J_{HH}$ 4.4 Hz, $^4J_{HH}$ 2.9 Hz, $^4J_{HH}$ 1.3 Hz, $^5J_{PH}$ 1.2 Hz, H-5), 5.79 (ddd, 1H, $^3J_{HH}$ 9.9 Hz, $^4J_{HH}$ 1.7 Hz, $^4J_{PH}$ 4.1 Hz, H-4), 6.10 (dddd, 1H, $^3J_{HH}$ 4.4 Hz, $^4J_{HH}$ 2.7 Hz, $^4J_{HH}$ 1.3 Hz, $^3J_{PH}$ 18.0 Hz, H-7), 7.14-7.59 (m, 20H, ArH). $^{13}$C{$^1$H} NMR δ 28.30 (d, $^2J_{PC}$ 3.6 Hz, C-8), 32.37 (d, $^2J_{PC}$ 6.0 Hz, C-10), 44.78 (d, $^2J_{PC}$ 19.8 Hz, C-3a), 46.22 (d, $^3J_{PC}$ 12.6 Hz, C-6), 52.71 (d, $^2J_{PC}$ 4.8 Hz, C-9), 70.07 (d, $^2J_{PC}$ 16.2 Hz, C-3), 80.53 (d, $^4J_{PC}$ 2.4 Hz, C-11), 125.43-128.78 (12CHAr, 2CH=), 130.10 (d, $^2J_{PC}$ 9.6 Hz, C-7), 135.46 (d, $^1J_{PC}$ 150.8 Hz, C-7a), 138.70 (d, $^3J_{PC}$ 3.0 Hz, C-21), 139.49 (d, $^3J_{PC}$ 4.8 Hz, C-17), 144.74 (C-13), 145.26 (C-13'). $^{31}$P{$^1$H} NMR δ 28.34. IR (KBr) 3193, 1203, 1172 cm$^{-1}$; MS (*m/z*) 547 (M+1, 100). Analysis: Calcd (%) for $C_{35}H_{35}N_2O_2P$ (546.24): C, 76.90; H, 6.45; N, 5.12. Found: C, 76.92; H, 6.42; N, 5.16.

**(1$R_p$*,3*R**,3a*S**,6*R**)-1-{1-[Benzyl(methyl)amino]-3-phenyl-2-methyl-1-oxido-2,3,3a,6-tetrahydro-1*H*-2,1-benzazaphosphol-6-yl}(diphenyl)methanol (epimer of 10c at the phosphorus atom).**

Yield after flash chromatography (ethyl acetate/hexene, 4:1) 18% (54 mg). Oil. $^1$H NMR δ 2.13 (bs, 1H, H-12, OH), 2.35 (d, 3H, $^3J_{PH}$ 8.9 Hz, H-8), 2.68 (d, 3H, $^3J_{PH}$ 9.7 Hz, H-10), 3.03 (m, 1H, H-3a), 3.82(d, 1H, $^3J_{HH}$ 9.7 Hz, H-3), 4.13 (m, 1H, H-6), 4.18 (dd, 1H, $^2J_{HH}$ 14.5 Hz, $^3J_{PH}$ 9.7 Hz, H-9), 4.42 (dd, 1H, $^2J_{HH}$ 14.5 Hz, $^3J_{PH}$ 8.1 Hz, H-9'), 5.58 (m, 1H, H-5), 5.65 (dc, 1H, $^3J_{HH}$ 10.3 Hz, $^{3,4}J_{HH}$ 2.3 Hz, $^4J_{PH}$ 2.3 Hz, H-4), 6.56 (m, 1H, $^3J_{PH}$ 17.8 Hz, H-7), 7.16-7.41 (m, 16H, ArH), 7.57 (d, 2H, $^3J_{HH}$ 7.3 Hz, H-14), 7.63 (d, 2H, $^3J_{HH}$ 7.3 Hz, H-14'). $^{13}$C{$^1$H} NMR δ 28.10 (d, $^2J_{PC}$ 1.5 Hz, C-8), 33.34 (d, $^2J_{PC}$ 5.4 Hz, C-10), 45.65 (d, $^2J_{PC}$ 12.6 Hz, C-6), 47.16 (d, $^3J_{PC}$ 16.8 Hz, C-3a), 52.57 (d, $^2J_{PC}$ 5.4 Hz, C-9), 67.35 (d, $^2J_{PC}$ 16.2 Hz, C-3), 79.46 (C-11), 125.15-128.83 (12CHAr, 2CH=), 134.59 (C-7), 134.75 (d, $^1J_{PC}$ 147.2 Hz, C-7a), 138.38 (d, $^3J_{PC}$ 3.0 Hz, C-21), 138.86 (d, $^3J_{PC}$ 9.6 Hz, C-17), 145.91 (C-13), 146.37 (C-13'). $^{31}$P{$^1$H} NMR δ 29.07. IR (KBr) 3270, 1172 cm$^{-1}$; MS (*m/z*) 547 (M+1, 100). Analysis: Calcd (%) for $C_{35}H_{35}N_2O_2P$ (546.24): C, 76.90; H, 6.45; N, 5.12. Found: C, 76.88; H, 6.44; N, 5.13.

**(1$R_P$*,3*S**,3a*S**,7a*S**)-*N*-benzyl-3-phenyl-*N*,2-dimethyl-5-methoxy-2,3,3a,7a-tetrahydro-1*H*-2,1-benzazaphosphol-1-amine 1-oxide (12).**

Yield after flash chromatography (ethyl acetate/hexene, 3:1) 60% (130 mg). Oil. $^1$H NMR δ 2.35 (d, 3H, $^3J_{PH}$ 7.4 Hz, H-8), 2.53 (d, 3H, $^3J_{PH}$ 9.0 Hz, H-10), 3.06-3.24 (m, 2H, H-3a, H-7a), 3.52 (s,

3H, H-11), 3.95 (t, 1H, $^3J_{HH}$ 6.4 Hz, $^3J_{PH}$ 6.4 Hz, H-3), 4.36 (d, 2H, $^3J_{PH}$ 8.7 Hz, H-9), 4.50 (m, 1H, H-4), 5.63 (dt, 1H, $^3J_{HH}$ 9.8 Hz, $^3J_{HH}$ 2.8 Hz, $^3J_{PH}$ 9.8 Hz, H-7), 5.82 (ddt, 1H, $^3J_{HH}$ 9.8 Hz, $^4J_{HH}$ 1.9 Hz, $^4J_{PH}$ 1.9 Hz, H-6), 7.26-7.47 (m, 10H, ArH). $^{13}C\{^1H\}$ NMR δ 28.44 (d, $^2J_{PC}$ 3.6 Hz, C-8), 33.53 (d, $^2J_{PC}$ 4.3 Hz, C-10), 36.88 (d, $^1J_{PC}$ 108.6 Hz, C-7a), 42.14 (d, $^2J_{PC}$ 4.3 Hz, C-3a), 53.32 (d, $^2J_{PC}$ 4.7 Hz, C-9), 54.25 (C-11), 71.56 (d, $^2J_{PC}$ 27.3 Hz, C-3), 92.36 (d, $^3J_{PC}$ 10.2 Hz, C-4), 123.28 (d, $^2J_{PC}$ 6.9 Hz, C-7), 124.31 (d, $^3J_{PC}$ 11.9 Hz, C-6), 127.23 (CHAr), 127.24 (CHAr), 127.71 (CHAr), 128.41 (CHAr), 128.55 (CHAr), 128.67 (CHAr), 138.75 (d, $^3J_{PC}$ 2.7 Hz, C-16), 140.51 (d, $^3J_{PC}$ 4.0 Hz, C-12), 153.26 (d, $^4J_{PC}$ 4.5 Hz, C-5). $^{31}P\{^1H\}$ NMR δ 47.49. IR (KBr) 1261, 1097 $cm^{-1}$; MS (*m/z*) 395 (M+1, 100). Analysis: Calcd (%) for $C_{23}H_{27}N_2O_2P$ (394.18): C, 70.03; H, 6.90; N, 7.10. Found: C, 70.08; H, 6.92; N, 7.13.

**(1*R*$_P$*,3*S**,3a*S**,9b*S**)-*N*-benzyl-3-phenyl-*N*,2-dimethyl-2,3,3a,9b-tetrahydro-1*H*-naphtho[1,2-*c*][1,2]azaphosphol-1-amine 1-oxide (14).**

Yield after flash chromatography (ethyl acetate/hexene, 1.5:1) 72% (164 mg). Oil. $^1H$ NMR δ 2.61 (d, 3H, $^3J_{PH}$ 7.6 Hz, H-10), 2.68 (d, 3H, $^3J_{PH}$ 9.2 Hz, H-12), 3.52 (ddt, 1H, $^3J_{HH}$ 18.5 Hz, $^3J_{HH}$ 6.6 Hz, $^4J_{HH}$ 2.3 Hz, H-3a), 3.62 (dd, 1H, $^3J_{HH}$ 18.5 Hz, $^2J_{PH}$ 35.2 Hz, H-9b), 4.10 (dd, 1H, $^2J_{HH}$ 14.4 Hz, $^3J_{PH}$ 7.9 Hz, H-11), 4.50 (m, 1H, $^3J_{HH}$ 6.6 Hz, $^3J_{PH}$ 15.2 Hz, H-3), 4.85 (dd, 1H, $^2J_{HH}$ 14.4 Hz, $^3J_{PH}$ 7.8 Hz, H-11'), 5.90 (m, 1H, $^3J_{HH}$ 9.7 Hz, H-4), 6.33 (dd, 1H, $^3J_{HH}$ 9.7 Hz, $^4J_{HH}$ 2.3 Hz, H-5), 7.08 (m, 1H, H-6), 7.21-7.48 (m, 9H, ArH), 7.55 (d, 2H, $^3J_{HH}$ 7.4 Hz, H-14). $^{13}C\{^1H\}$ NMR δ 28.69 (d, $^2J_{PC}$ 3.0 Hz, C-10), 33.97 (d, $^2J_{PC}$ 4.8 Hz, C-12), 38.72 (d, $^1J_{PC}$ 117.7 Hz, C-9b), 43.05 (d, $^2J_{PC}$ 5.4 Hz, C-3a), 53.63 (d, $^2J_{PC}$ 5.4 Hz, C-11), 65.00 (d, $^2J_{PC}$ 12.6 Hz, C-3), 126.29 (d, $^3J_{PC}$ 6.0 Hz, C-9), 126.89 (d, $^4J_{PC}$ 1.2 Hz, C-6), 127.17 (CHAr), 127.22 (CHAr), 127.37 (CHAr), 127.57 (CHAr), 127.67 (CHAr), 127.80 (C-4), 127.86 (CHAr), 127.91 (C-14), 128.30 (CHAr), 128.37 (CHAr), 128.73 (C-18), 129.35 (d, $^4J_{PC}$ 1.2 Hz, C-5), 131.56 (d, $^2J_{PC}$ 1.2 Hz, C-9a), 134.38 (d, $^3J_{PC}$ 9.6 Hz, C-5a), 137.09 (C-13), 138.48 (d, $^3J_{PC}$ 3.6 Hz, C-17). $^{31}P\{^1H\}$ NMR δ 37.90. IR (KBr) 1198, 1173 $cm^{-1}$; MS (*m/z*) 415 (M+1, 100). Analysis: Calcd (%) for $C_{26}H_{27}N_2OP$ (414.19): C, 75.34; H, 6.57; N, 6.76. Found: C, 75.36; H, 6.52; N, 6.73.

**General procedure for the preparation of *N*-methyl-*γ*-aminophosphonic acids 16 and 17a-b.**

To a solution of the appropriated benzazaphosphole (**8a**, **10a-b**) ($2.74 \times 10^{-4}$ mol) in acetone (5 mL), 2N HCl (0.14 mL) was added at room temperature. The mixture reaction was stirred 3 days at room temperature. Then, mixture reaction was treated with 1N NaOH until neutral pH and extracted with ethyl acetate (1x10 mL). The aqueous layers were concentrated in vacuo. Then, MeOH (5 mL) was added, and the NaCl from aqueous layers filtered. MeOH solution was dried over $Na_2SO_4$, filtered and to afford aminophosphonic acids **16** and **17a-b**.

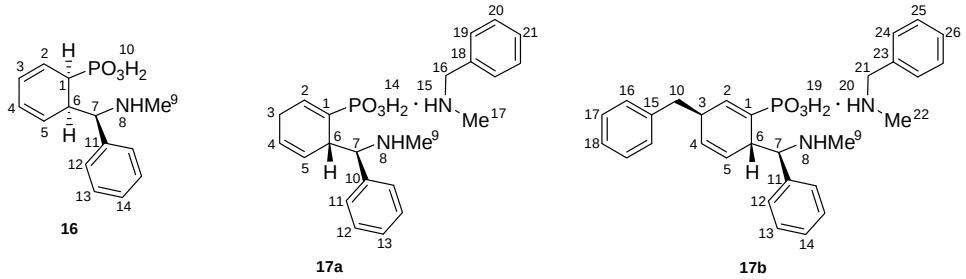


**Chart S3**. Scheme numbering used for the NMR assignments of phosphonic acids **16** and **17a-b**.

**{(1*R**,6*R**)-6-{(*R**)[(methylamino)(phenyl)]methyl}cyclohexa-2,4-dien-1-yl}phosphonic acid (16).**

Crude reaction. Oil. $^{1}$H NMR ($D_2O$) δ 2.30 (s, 3H, H-9), 2.95 (m, 1H, $^{2}J_{PH}$ 24.2 Hz, H-2), 3.37 (m, 1H, $^{3}J_{PH}$ 34.2 Hz, H-6), 4.31 (d, 1H, $^{3}J_{HH}$ 11.1 Hz, H-7), 4.70 (s, OH, NH), 5.38 (dd, 1H, $^{3}J_{HH}$ 9.9 Hz, $^{3}J_{HH}$ 3.4 Hz, H-5), 6.02 (m, 1H, H-4), 6.24 (m, 2H, H-2, H-3), 7.62-7.73 (m, 5H, ArH). $^{13}$C{$^{1}$H} NMR ($D_2O$) δ 32.16 (C-9), 38.13 (d, $^{1}J_{PC}$ 120.3 Hz, C-1), 40.86 (d, $^{2}J_{PC}$ 3.8 Hz, C-6), 64.11 (d, $^{3}J_{PC}$ 3.5 Hz, C-7), 124.61 (d, $^{3}J_{PC}$ 10.9 Hz, C-3), 124.73 (d, $^{4}J_{PC}$ 4.8 Hz, C-4), 127.40 (d, $^{3}J_{PC}$ 8.2 Hz, C-5), 128.62 (CHAr), 129.16 (d, $^{2}J_{PC}$ 8.2 Hz, C-2), 129.17 (CHAr), 129.61 (CHAr), 139.29 (C-11). $^{31}$P{$^{1}$H} NMR ($D_2O$) δ 19.00. MS (*m/z*) 280 (M+1, 100). Analysis: Calcd (%) for $C_{11}H_{24}NO_3P$ (279.10): C, 60.21; H, 6.50; N, 5.02. Found: C, 60.25; H, 6.52; N, 5.00.

***N*-benzyl-*N*-methylamine {(*R**)-6-{(*S**)[(methylamino)(phenyl)]methyl}cyclohexa-1,4-dien-1-yl}monophosphonate (17a).** Crude reaction. Identified from the complex **17a**·*N,N'*-benzylmethylamine. Oil. $^{1}$H NMR ($D_2O$) δ 1.86 (m, 1H, H-3), 2.38 (dddd, 1H, $^{2}J_{HH}$ 23.0 Hz, $^{3}J_{HH}$ 8.5 Hz, $^{3}J_{HH}$ 5.2 Hz, $^{4}J_{HH}$ 2.8 Hz, H-3'), 2.40 (s, 3H, H-9), 2.60 (s, 3H, amine), 3.72 (m, 1H, H-6), 4.08 (s, 2H, amine), 4.16 (d, 1H, $^{3}J_{HH}$ 6.9 Hz, H-7), 4.67 (s, OH, NH), 5.43 (m, 1H, H-5), 5.69 (dd, 1H, $^{3}J_{HH}$ 9.5 Hz, $^{3}J_{HH}$ 4.2 Hz, H-4), 5.97 (dd, 1H, $^{3}J_{HH}$ 5.2 Hz, $^{3}J_{PH}$ 19.0 Hz, H-2), 7.28 (m, 5H, ArH of amine), 7.33-7.38 (m, 5H, ArH). $^{13}$C{$^{1}$H} NMR ($D_2O$) δ 26.77 (d, $^{3}J_{PC}$ 13.7 Hz, C-3), 31.45 (C-9), 32.13 (amine), 39.15 (d, $^{2}J_{PC}$ 11.3 Hz, C-6), 52.21 (amine), 67.85 (C-7), 123.45 (d, $J_{PC}$ 8.0 Hz, CH=), 128.57-129.81 (6CHAr, 1CH=), 130.62 (CHAr amine), 132.31 (C-10), 133.32 (d, $^{1}J_{PC}$ 171.2 Hz, C-1), 138.67 (d, $^{2}J_{PC}$ 8.4 Hz, C-2). $^{31}$P{$^{1}$H} NMR ($D_2O$) δ 11.27. IR (KBr) 3413, 1624, 1130 cm$^{-1}$; MS (*m/z*) 280 (M+1, 100), 122 (M+1 (amine)). Analysis: Calcd (%) for $C_{11}H_{24}NO_3P$ (279.10): C, 60.21; H, 6.50; N, 5.02. Found: C, 60.27; H, 6.54; N, 5.06.

***N*-benzyl-*N*-methylamine [(3*R**,6*S**)-3-Benzyl-6-{(*R**)-[(methylamine)(phenyl)]methyl]}-cyclohexa-1,4-dien-1-yl]monophosphonate (17b).**

Crude reaction. Identified from the complex **17b**·*N,N'*-benzylmethylamine, ratio 63:37. Oil. $^{1}$H NMR (500.13 MHz, MeOH-$d_4$) δ 2.40 (s, 3H, H-9), 2.55-2.60 (m, 2H, H-3, H-10), 2.66 (s, 1.73H, H-22), 2.69 (m, 1H, H-10'), 3.97 (m, 1H, H-6), 4.09 (d, 1H, $^{3}J_{HH}$ 7.9 Hz, H-7), 5.06 (s, 1.15H, H-21), 5.06 (s, OH, NH), 5.41 (dddd, 1H, $^{3}J_{HH}$ 9.8 Hz, $^{3}J_{HH}$ 5.0 Hz, $^{4}J_{HH}$ 2.6 Hz, $^{4}J_{PH}$ 4.0 Hz, H-5), 5.65 (dt, 1H,

$^{3}J_{HH}$ 9.8 Hz, $^{4}J_{HH}$ 1.5 Hz, H-4), 6.71 (dt, 1H, $^{3}J_{HH}$ 18.7 Hz, $^{4}J_{HH}$ 1.7 Hz, $^{3}J_{PH}$ 18.7 Hz, H-2), 6.68-6.73 (m, 3H, H-16, H-18), 7.14-7.16 (m, 2H, H-17), 7.39-7.41 (m, 3H, H-13, H-14), 7.43-7.45 (m, 1.73H, H-25, H-26), 7.45-7.48 (m, 2H, H-12), 7.54 (m, 1.15H, H-24). $^{13}C\{^{1}H\}$ NMR (125.76 MHz, MeOH-$d_4$) δ 31.95 (C-9), 32.99 (C-22), 38.74 (d, $^{3}J_{PC}$ 13.0 Hz, C-3), 41.56 (d, $^{2}J_{PC}$ 11.5 Hz, C-6), 42.20 (C-10), 53.41 (C-21), 70.04 (C-7), 126.23 (d, $^{3}J_{PC}$ 8.6 Hz, C-5), 127.17-130.93 (CHAr), 133.07 (d, $^{4}J_{PC}$ 3.4 Hz, C-4), 133.08 (C-23), 135.32 (C-11), 136.35 (d, $^{1}J_{PC}$ 167.5 Hz, C-1), 140.75 (C-15), 141.48 (d, $^{2}J_{PC}$ 7.8 Hz, C-2). $^{31}P\{^{1}H\}$ NMR (202.46 MHz, MeOH-$d_4$) δ 12.41. IR (KBr) 3399, 1629, 1052 $cm^{-1}$; MS (*m/z*) 370 (M+1, 100) (phosphonic acid). Analysis: Calcd (%) for $C_{21}H_{24}NO_3P$. (369.15): C, 68.28; H, 6.55; N, 3.79. Found: C, 68.27; H, 6.54; N, 3.75.

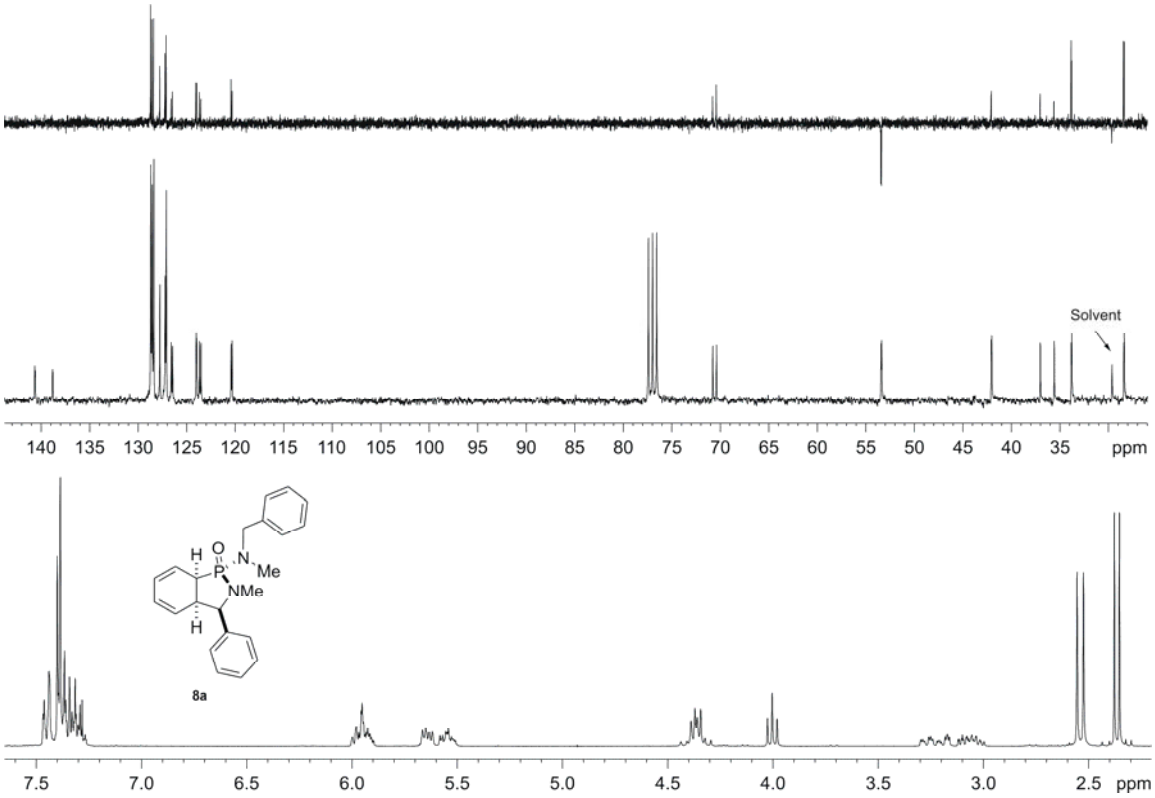


**Figure S1.** $^{1}H$ NMR (bottom) (300.13 MHz) and $^{13}C\{^{1}H\}$(middle) and DEPT-135 (top) NMR spectra (75.47 MHz) of **8a** measured in $CDCl_3$.

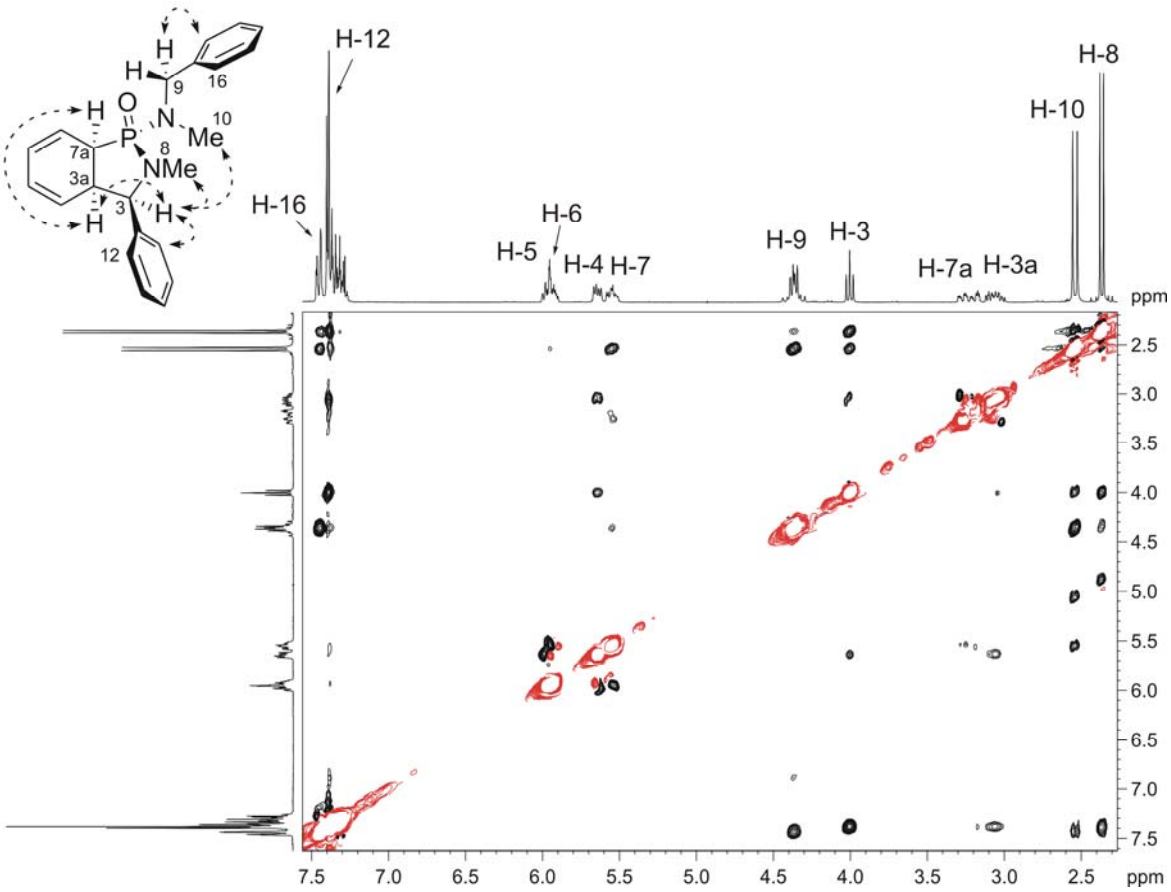


**Figure S2.** 2D gNOESY spectrum (300.13 MHz, mixing time 0.5 s) of **8a** and selected NOEs observed that confirm the assignment of the relative configuration of the stereogenic centers.

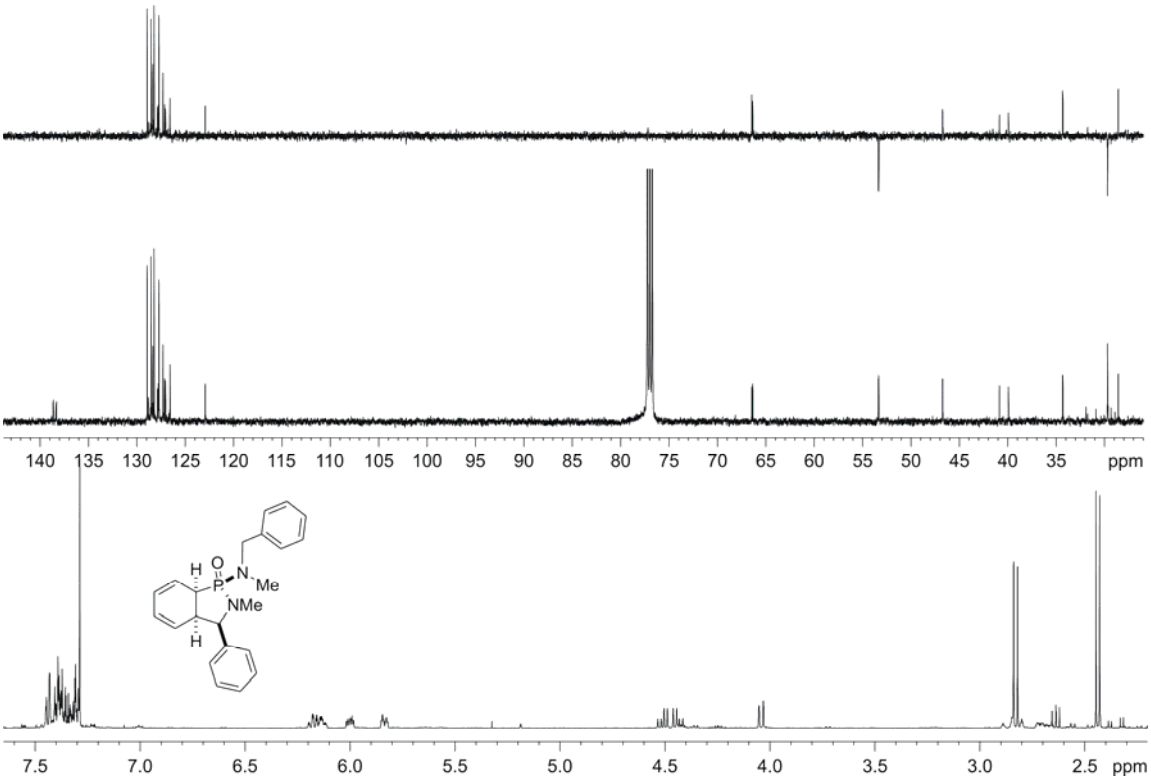


**Figure S3.** $^{1}$H NMR (bottom) (500.13 MHz) and $^{13}$C{$^{1}$H}(middle) and DEPT-135 (top) NMR spectra (125.76 MHz) of the epimer of **8a** at the phosphorus atom measured in $CDCl_3$.

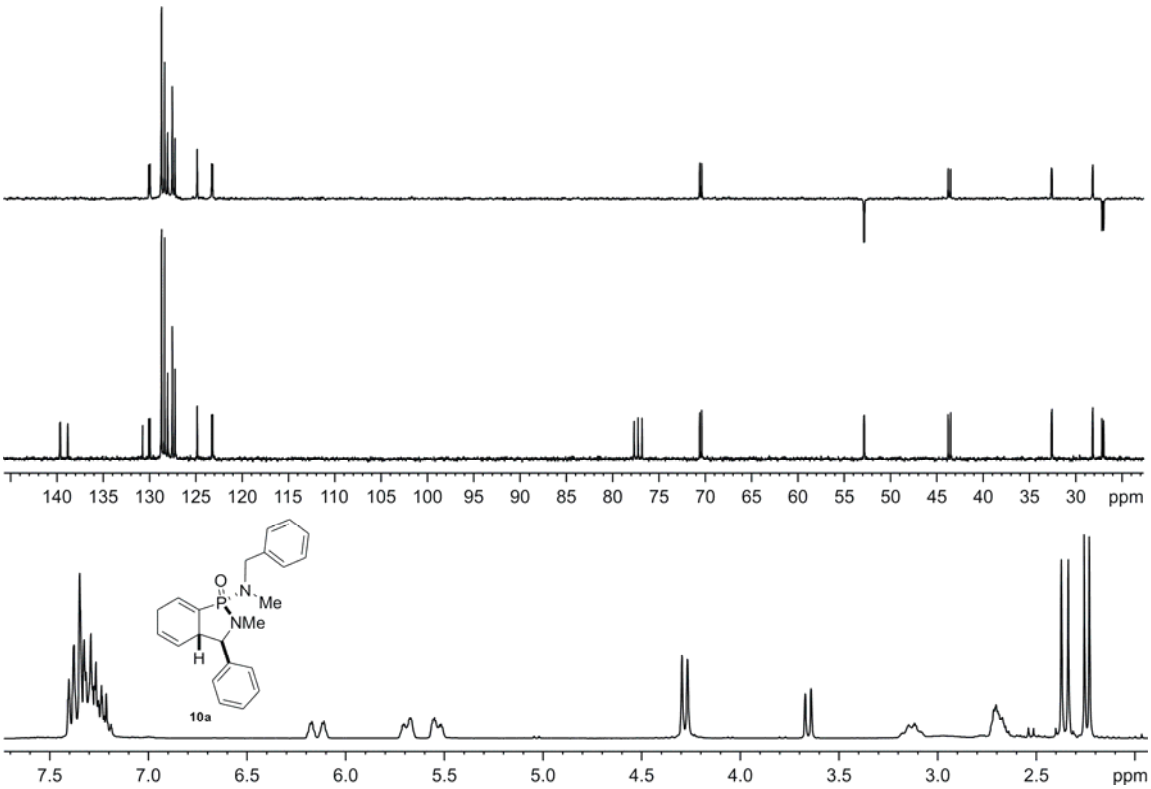


**Figure S4.** $^{1}$H NMR (bottom) (300.13 MHz) and $^{13}$C{$^{1}$H}(middle) and DEPT-135 (top) NMR spectra (75.47 MHz) of **10a** measured in $CDCl_3$.

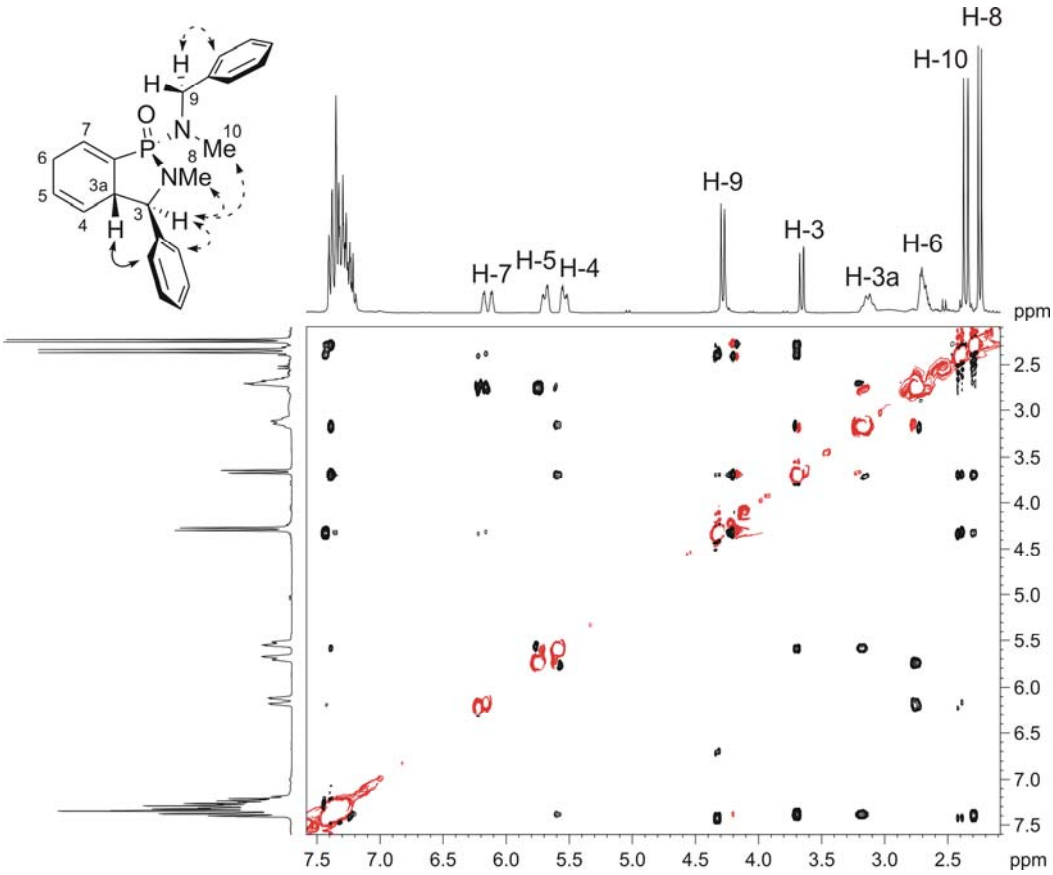


**Figure S5.** 2D gNOESY spectrum (300.13 MHz, mixing time 0.5 s) of **10a** and selected NOEs observed that confirm the assignment of the relative configuration of the stereogenic centers.

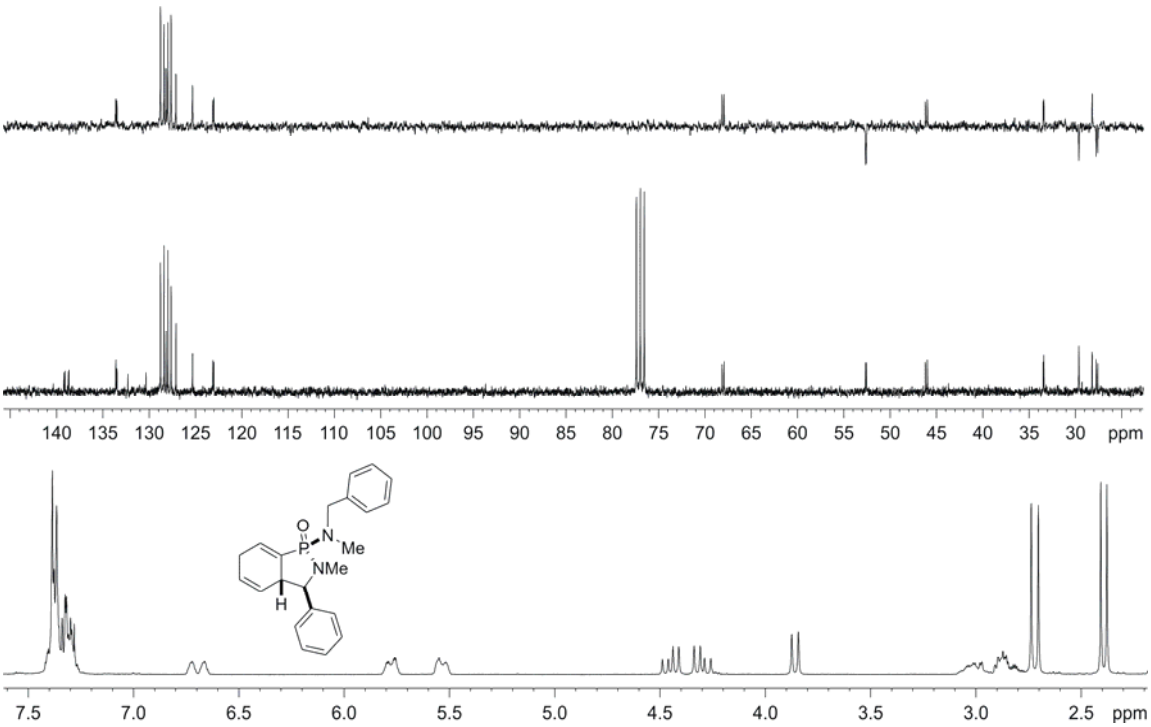


**Figure S6.** $^{1}$H NMR (bottom) (300.13 MHz) and $^{13}$C{$^{1}$H}(middle) and DEPT-135 (top) NMR spectra (75.47 MHz) of the epimer of **10a** at the phosphorus atom measured in $CDCl_3$.

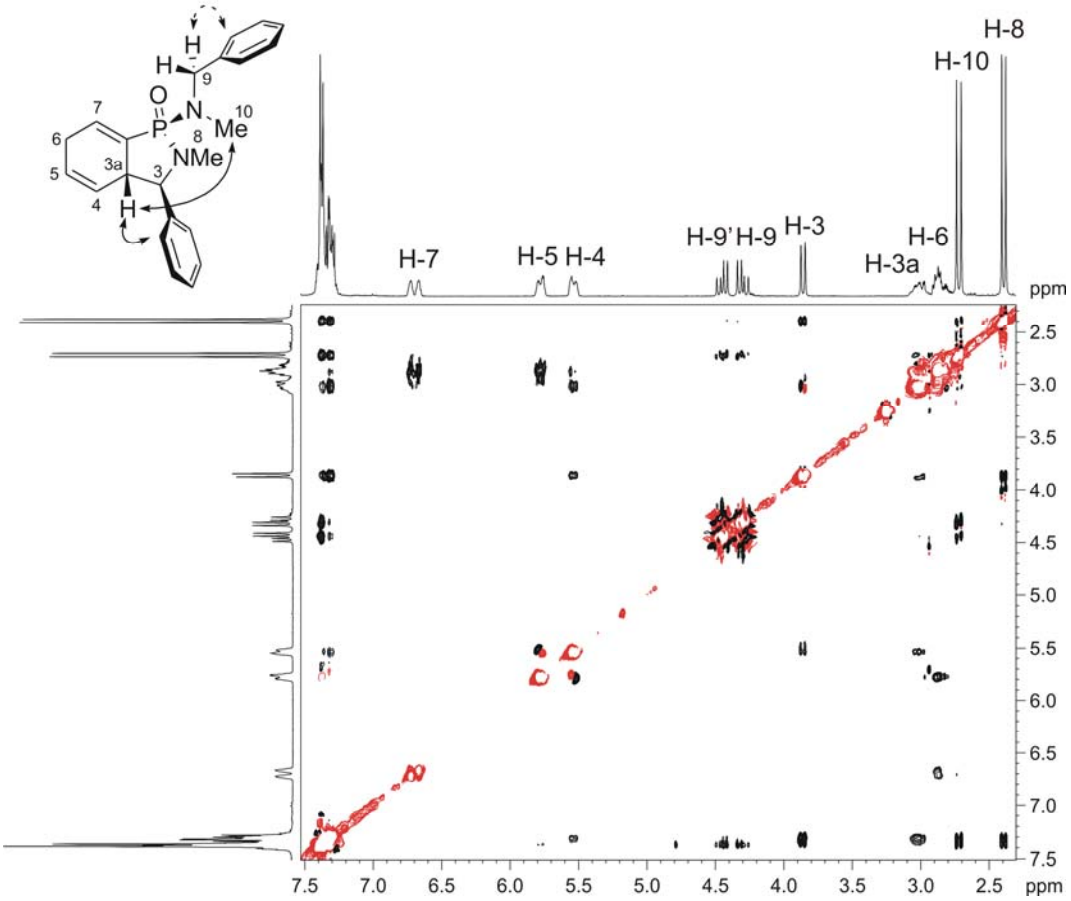


**Figure S7.** 2D gNOESY spectrum (300.13 MHz, mixing time 0.5 s) of the epimer of **10a** at the phosphorus atom and selected NOEs observed that confirm the assignment of the relative configuration of the stereogenic centers.

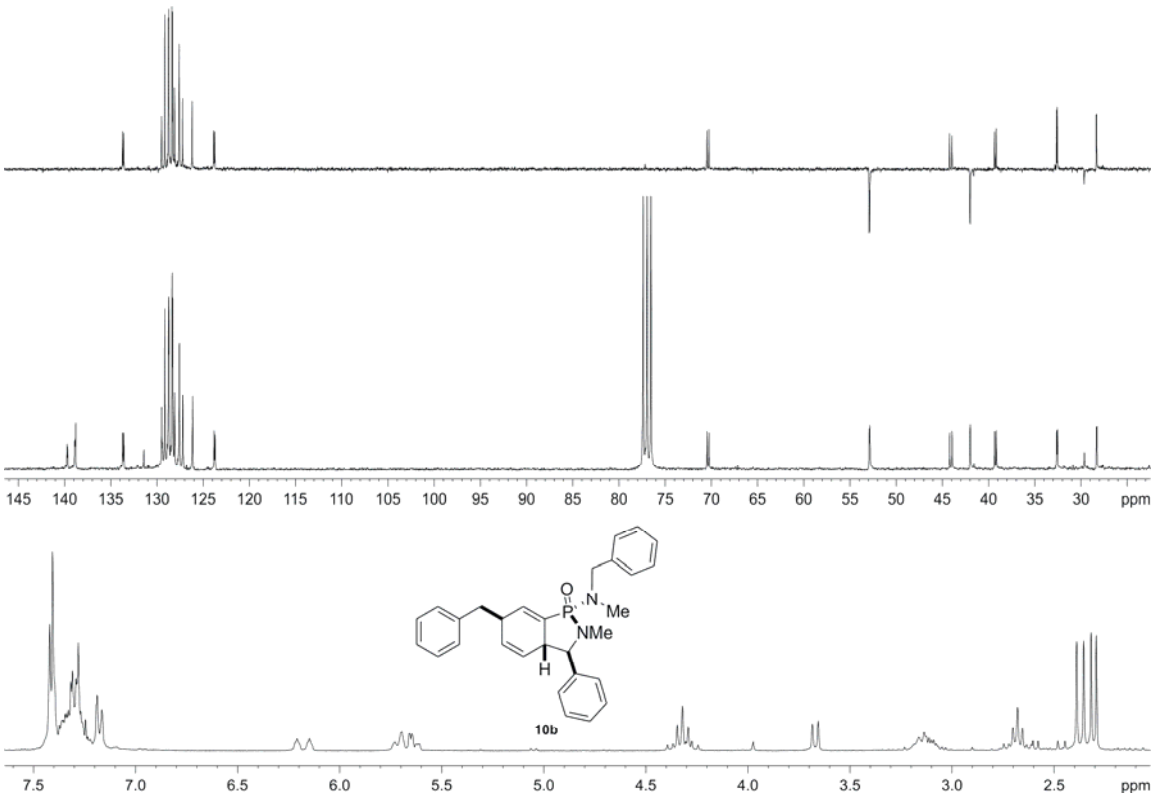


**Figure S8.** $^{1}$H NMR (bottom) (300.13 MHz) and $^{13}$C{$^{1}$H}(middle) and DEPT-135 (top) NMR spectra (75.47 MHz) of **10b** measured in $CDCl_3$.

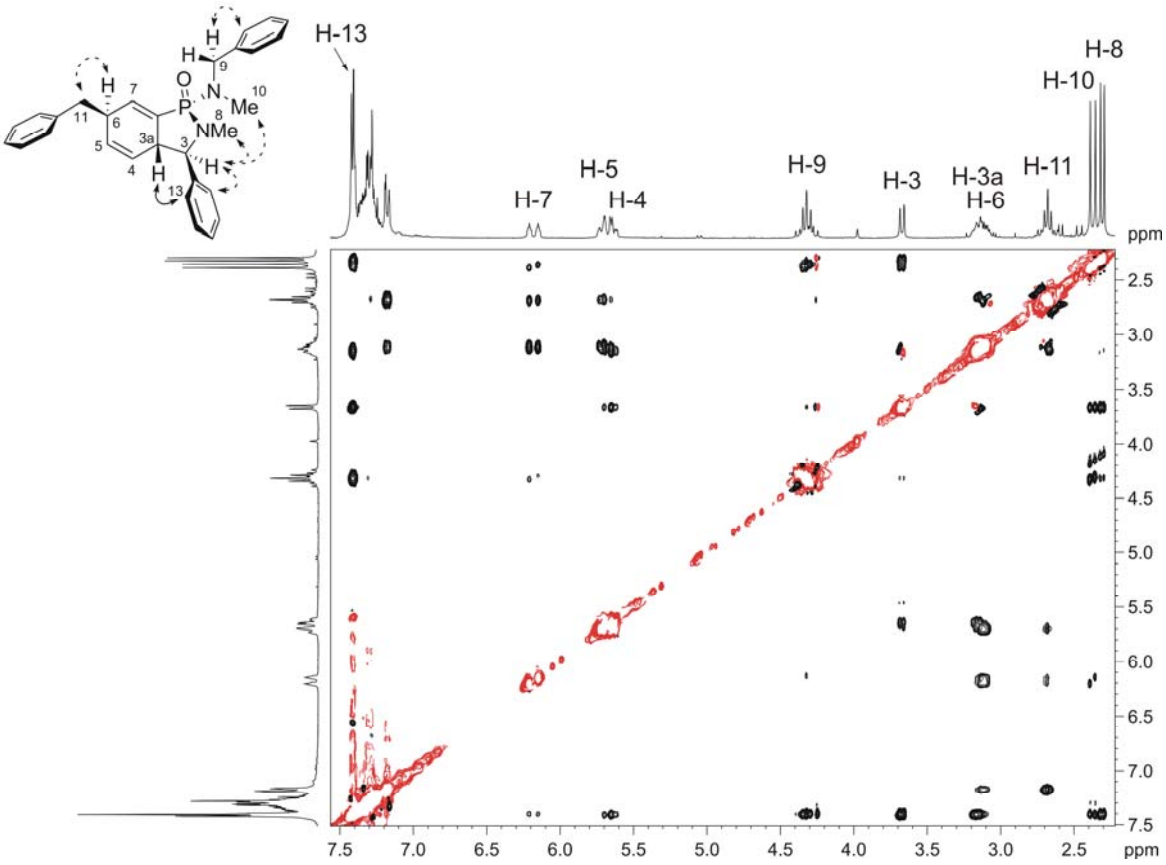


**Figure S9.** 2D gNOESY spectrum (300.13 MHz, mixing time 0.5 s) of **10b** atom and selected NOEs observed that confirm the assignment of the relative configuration of the stereogenic centers.

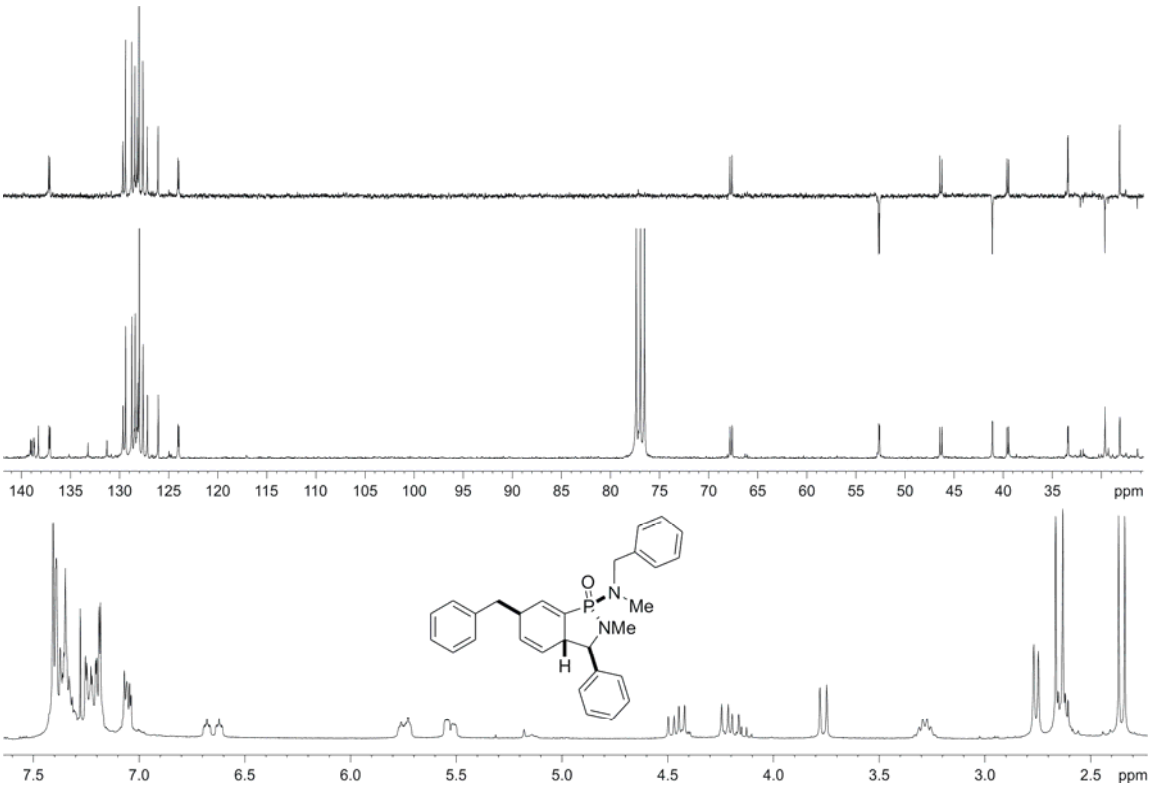


**Figure S10.** $^{1}$H NMR (bottom) (300.13 MHz) and $^{13}$C{$^{1}$H}(middle) and DEPT-135 (top) NMR spectra (75.47 MHz) of the epimer of **10b** at the phosphorus atom measured in $CDCl_3$.

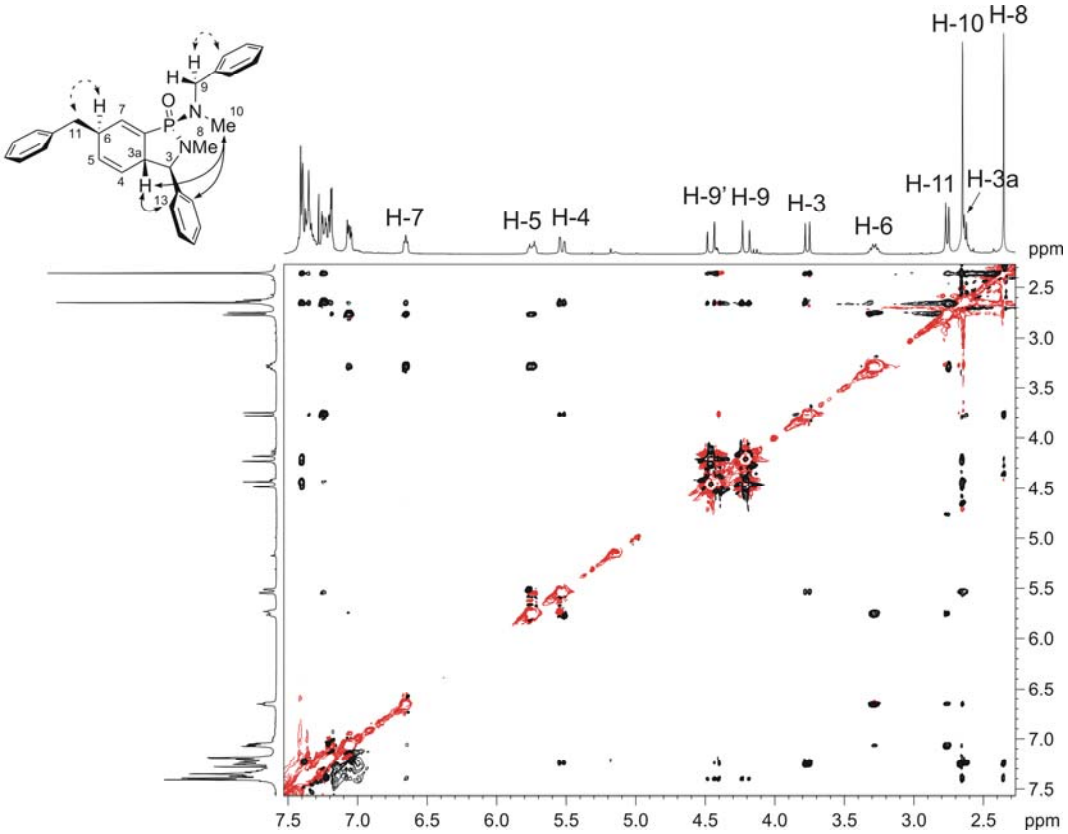


**Figure S11.** 2D $^{1}$H{$^{31}$P},$^{1}$H{$^{31}$P} gNOESY spectrum (300.13 MHz, mixing time 0.5 s) of the epimer of **10b** at the phosphorus atom and selected NOEs observed that confirm the assignment of the relative configuration of the stereogenic centers.

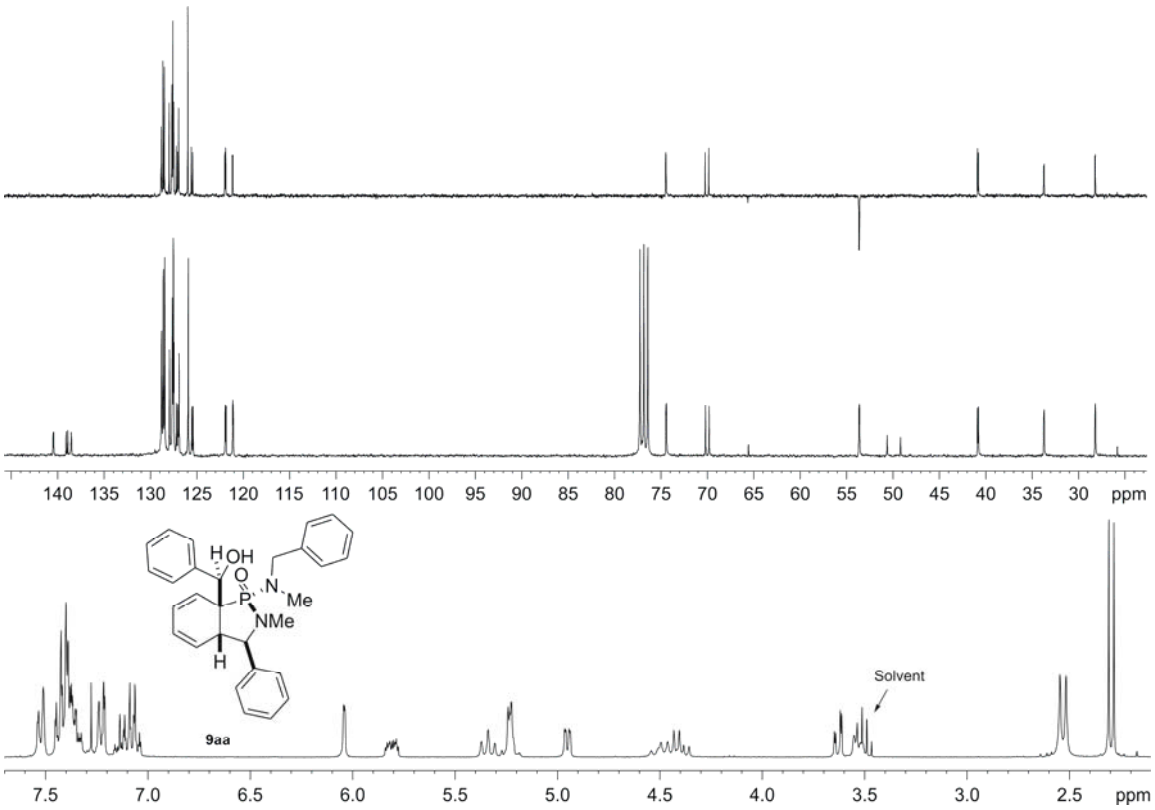


**Figure S12.** $^{1}$H NMR (bottom) (300.13 MHz) and $^{13}$C{$^{1}$H}(middle) and DEPT-135 (top) NMR spectra (75.47 MHz) of **9aa** measured in $CDCl_3$ at 55 ºC.

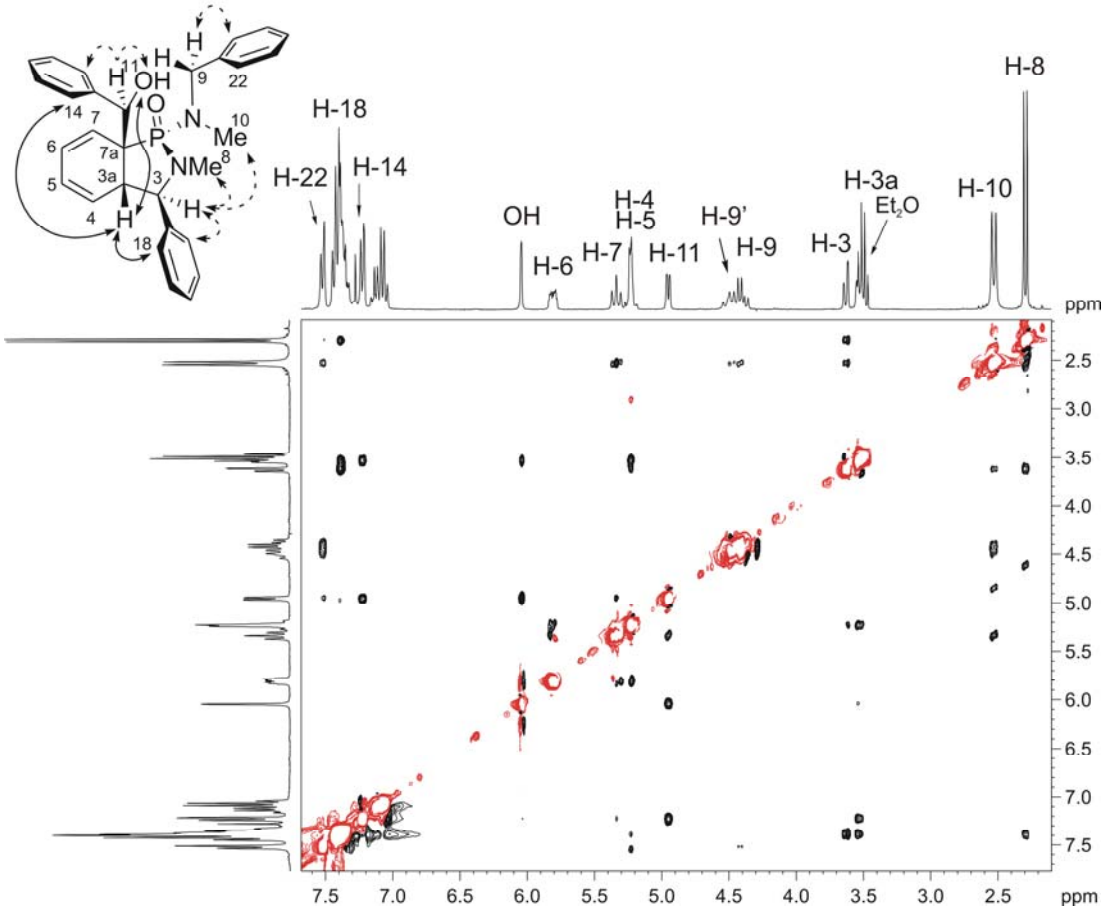


**Figure S13.** 2D gNOESY spectrum (300.13 MHz, mixing time 0.5 s) at 55 ºC of **9aa** and selected NOEs observed that confirm the assignment of the relative configuration of the stereogenic centers.

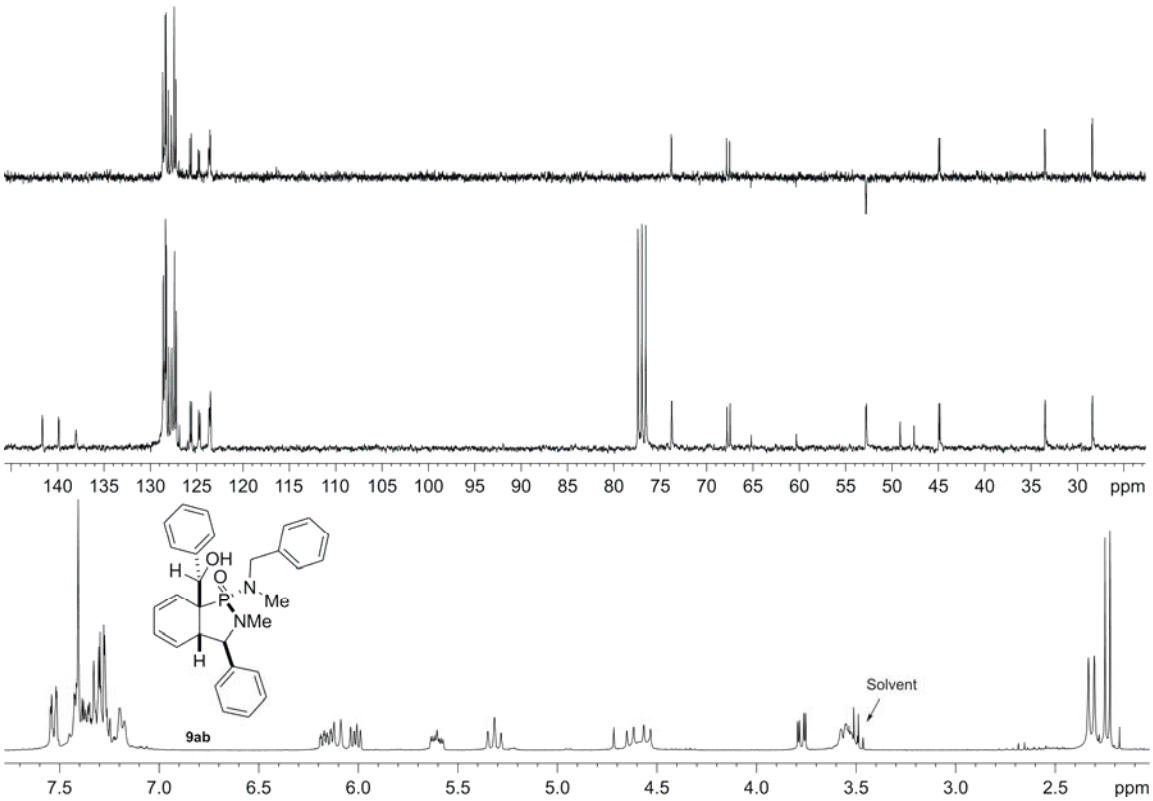


**Figure S14.** $^{1}$H NMR (bottom) (300.13 MHz) at 60 ºC and $^{13}$C{$^{1}$H}(middle) and DEPT-135 (top) NMR spectra (75.47 MHz) at 22 ºC of **9ab** measured in $CDCl_3$.

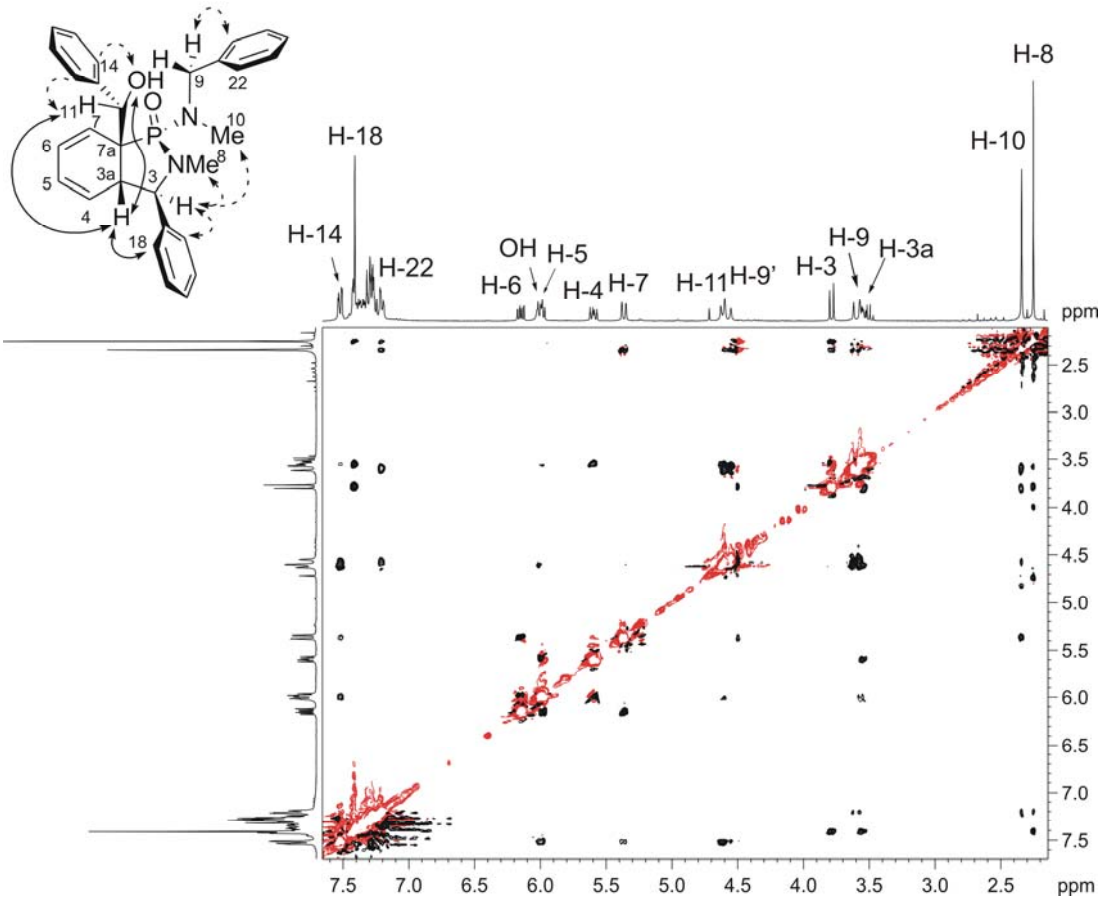


**Figure S15.** 2D $^{1}$H{$^{31}$P},$^{1}$H{$^{31}$P} gNOESY spectrum (300.13 MHz, mixing time 0.5 s) at 60 ºC of **9ab** and selected NOEs observed that confirm the assignment of the relative configuration of the stereogenic centers.

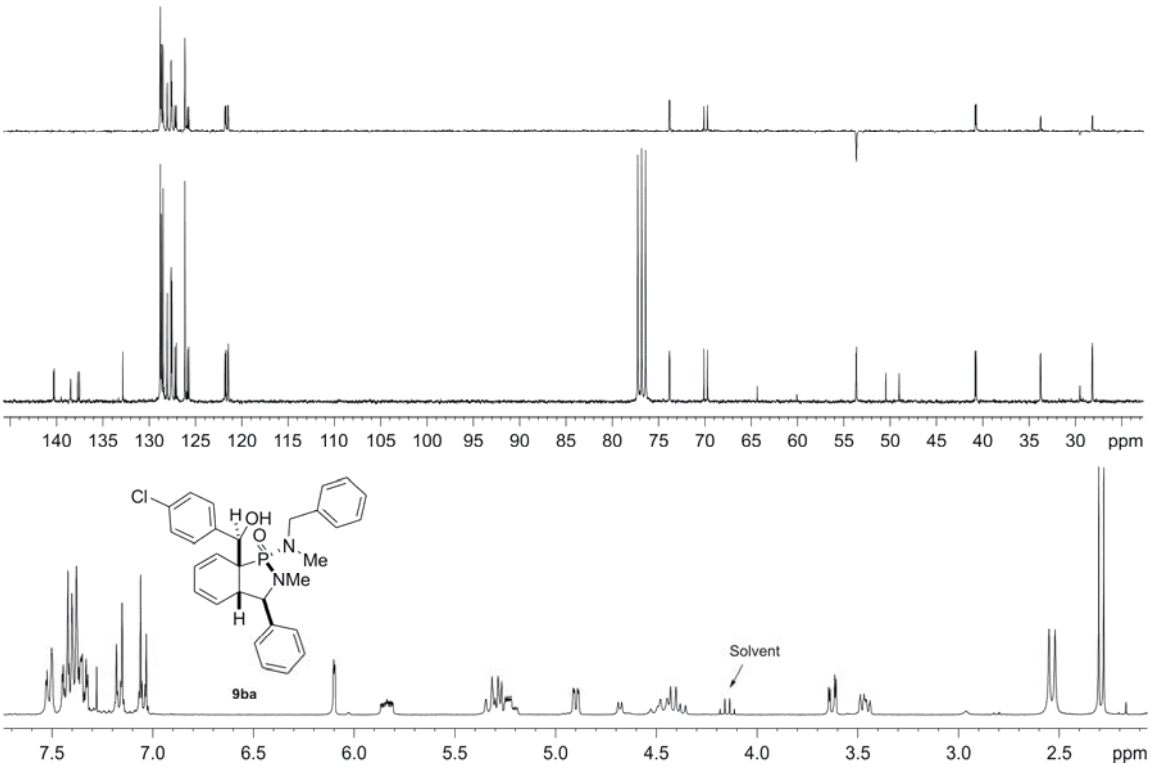


**Figure S16.** $^{1}$H NMR (bottom) (300.13 MHz) and $^{13}$C{$^{1}$H}(middle) and DEPT-135 (top) NMR spectra (75.47 MHz) of **9ba** measured in $CDCl_3$ at 60 ºC.

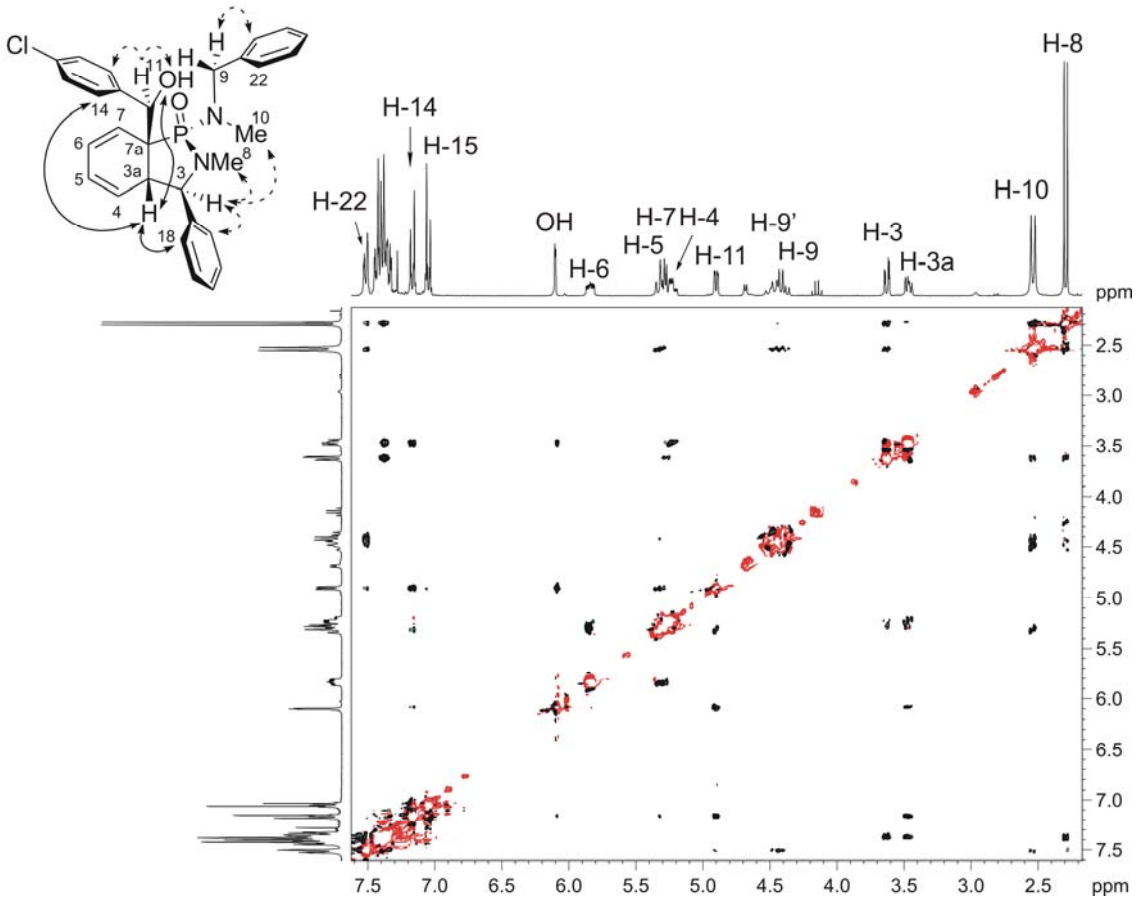


**Figure S17.** 2D gNOESY spectrum (300.13 MHz, mixing time 0.5 s) at 60 ºC of **9ba** and selected NOEs observed that confirm the assignment of the relative configuration of the stereogenic centers.

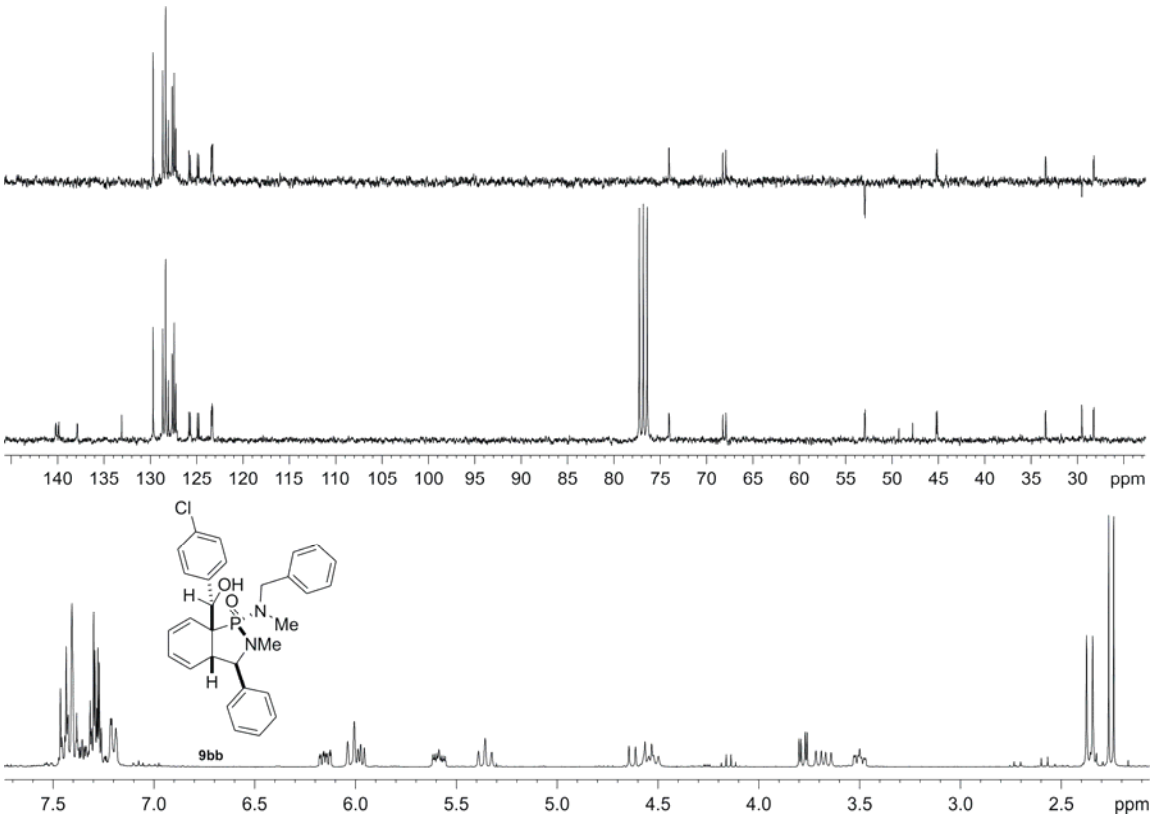


**Figure S18.** $^{1}$H NMR (bottom) (300.13 MHz) and $^{13}$C{$^{1}$H}(middle) and DEPT-135 (top) NMR spectra (75.47 MHz) of **9bb** measured in $CDCl_3$ at 55 ºC.

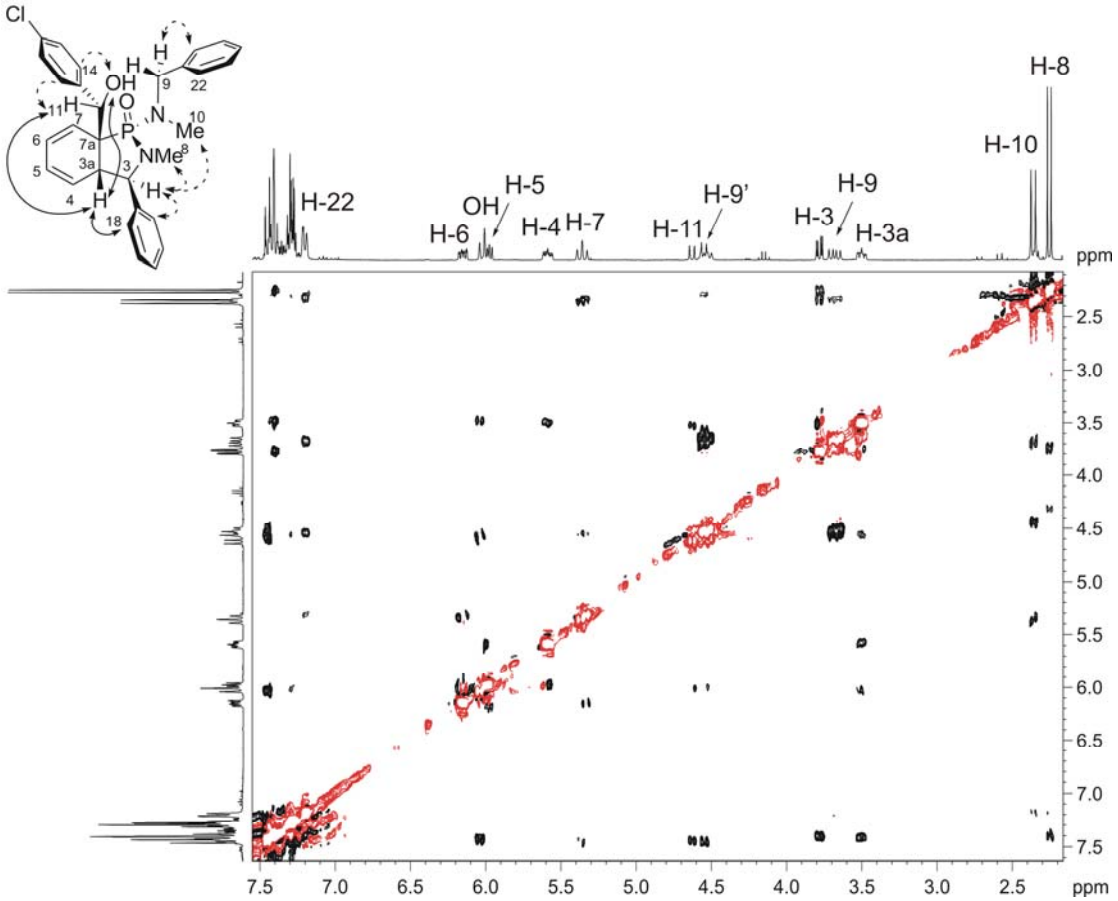


**Figure S19.** 2D gNOESY spectrum (300.13 MHz, mixing time 0.5 s) at 55 ºC of **9bb** and selected NOEs observed that confirm the assignment of the relative configuration of the stereogenic centers.

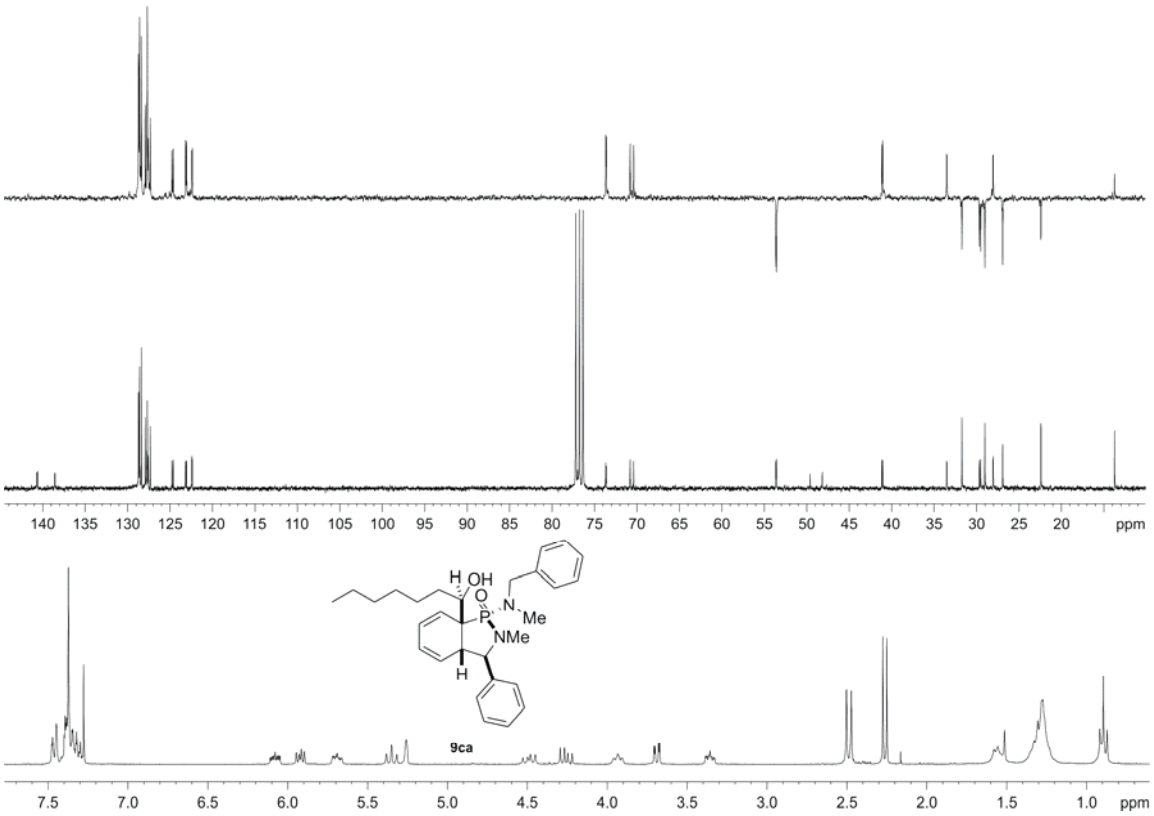


**Figure S20.** $^{1}$H NMR (bottom) (300.13 MHz) and $^{13}$C{$^{1}$H}(middle) and DEPT-135 (top) NMR spectra (75.47 MHz) of **9ca** measured in $CDCl_3$ at 60 ºC.

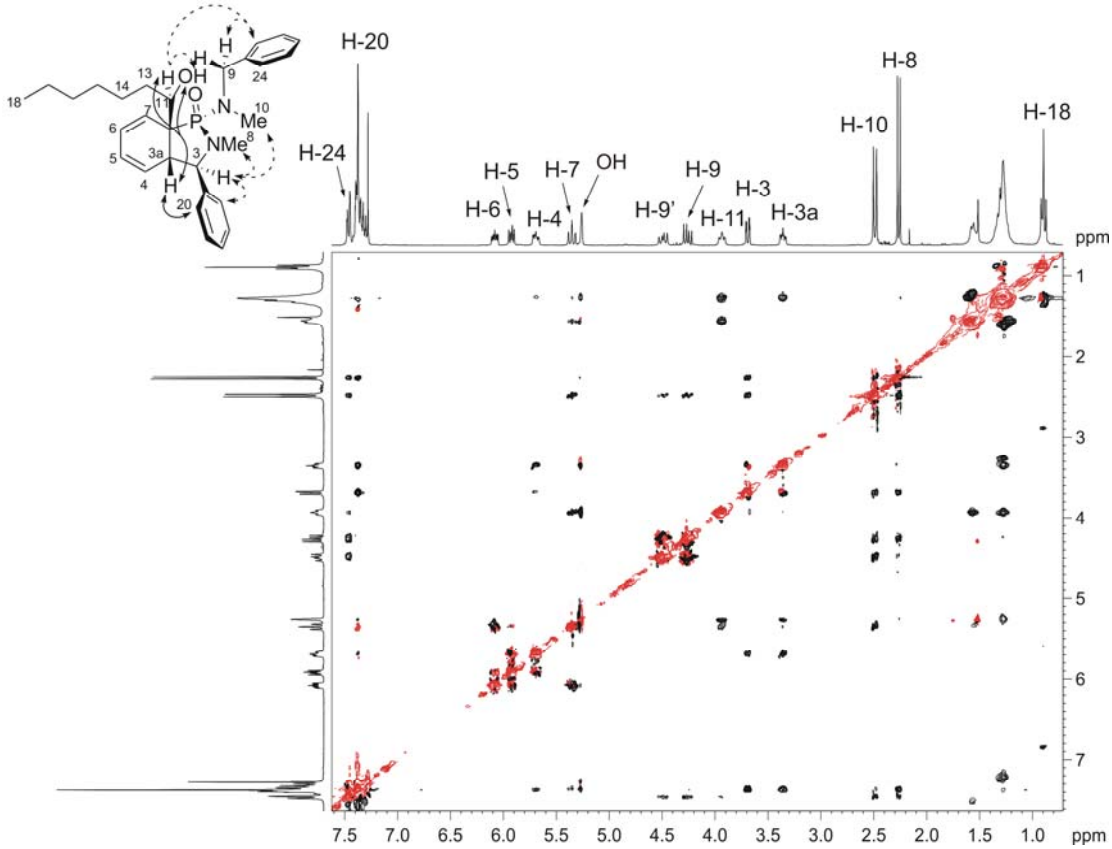


**Figure S21.** 2D gNOESY spectrum (300.13 MHz, mixing time 0.5 s) at 60 ºC of **9ca** and selected NOEs observed that confirm the assignment of the relative configuration of the stereogenic centers.

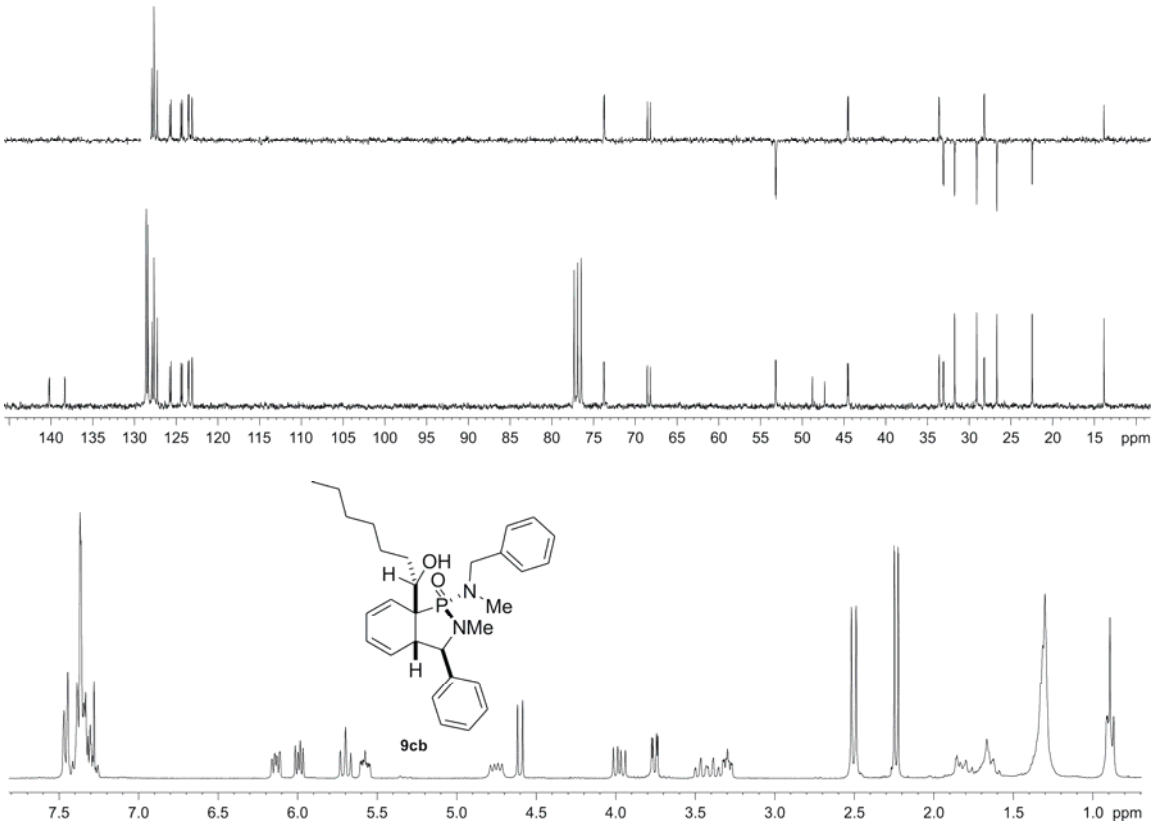


**Figure S22.** $^{1}$H NMR (bottom) (300.13 MHz) and $^{13}$C{$^{1}$H}(middle) and DEPT-135 (top) NMR spectra (75.47 MHz) of **9cb** measured in $CDCl_3$ at 45 ºC.

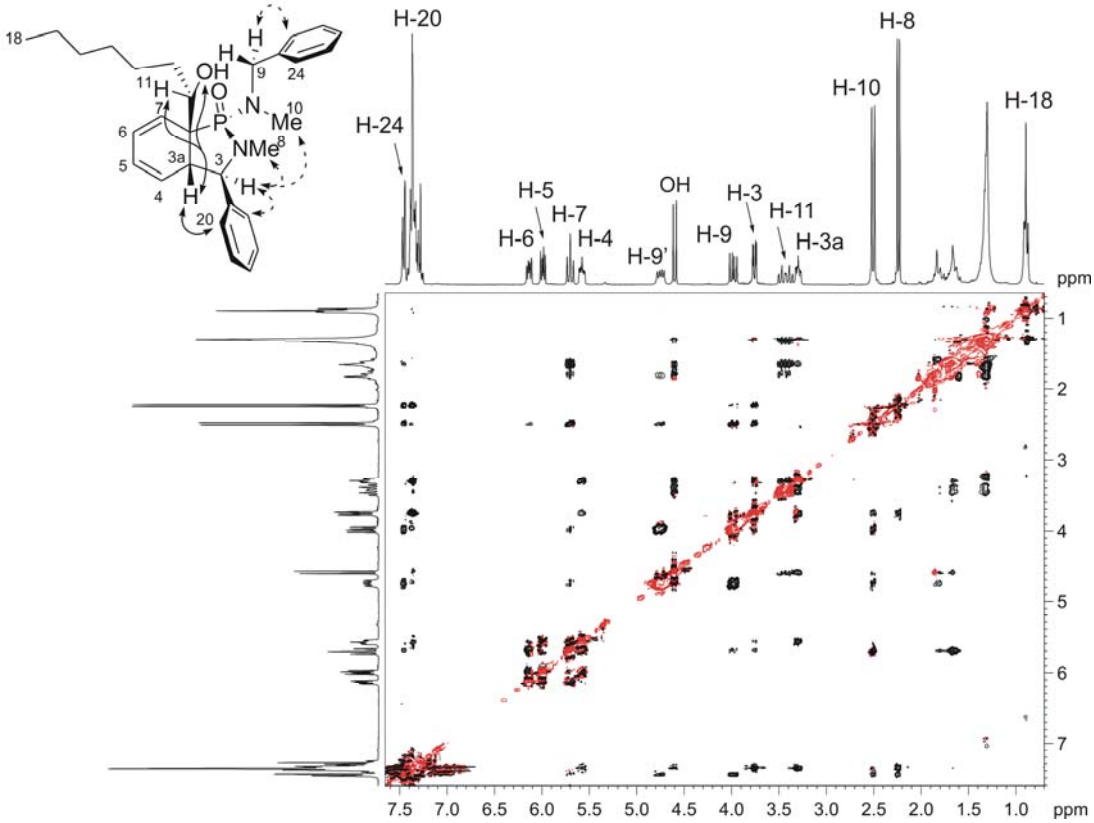


**Figure S23.** 2D gNOESY spectrum (300.13 MHz, mixing time 0.5 s) at 45 ºC of **9cb** and selected NOEs observed that confirm the assignment of the relative configuration of the stereogenic centers.

**References**

(1) Cascarano, G.; Altomare, A.; Giacovazzo, C.; Guagliardi, A.; Moliterni, A. G. G.; Siliqi, D.; Burla, M. C.; Polidori, G.; Camalli, M. *Acta Cryst. A* **1996**, *52*, C-79.

(2) G. M. Sheldrick, SHELXS-97. *Program for the Solution of Crystal Structures*, University of Göttingen, 1997.

(3) Boyd, M. R.; Paull, K. D. Some practical considerations and applications of the National Cancer Institute *in vitro* anticancer drug discovery screen, *Drug Dev. Res.* **1995**, *34*, 91-104.

(4) Droadhurst, M. D.; Tsang, T. H.; Tomko, J. *Patent No.* US 5186733, **1993**.