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Dynamic covalent chemistry approach toward 18-membered P_4N_2 macrocycles and their nickel(II) complexes

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Abstract. A dynamic covalent chemistry approach was used for the stereoselective synthesis of 1,10-diaza-3,8,12,17-tetraphosphacyclooctadecanes *via* condensation reaction of 1,4-bis(organylphosphino)butane, formaldehyde and primary amines. The obtained 18-membered P_4N_2 macrocycles were isolated in pure form as *meso*- ($R_PS_PS_PR_P$) or *rac*- ($R_PR_PR_PR_P$/$S_PS_PS_PS_P$) isomers. The structural features of the individual stereoisomers were revealed by NMR spectroscopy and X-ray structure analysis. All P_4N_2 macrocycles form square-planar nickel(II) complexes with the $R_PS_PS_PR_P$ isomer only, in which the orientation of the lone pairs of electrons at phosphorus favors this coordination mode, independent of the initial configuration of the ligand, indicating the ability of the 18-membered P_4N_2 macrocycles to stereoisomerise in the course of the complexation.

Introduction

Macroheterocyclic compounds are of particular interest due to their ability to isolate, separate and transfer different ions. Thus, they are able to increase the solubility of inorganic salts in organic solvents and activate the anion. These properties are the reason for their application as highly selective receptors, molecular containers and reactors, as well as catalytic systems,[1-5] and their use in organic and inorganic synthesis, biochemistry and biophysics, medicine, polymer chemistry, etc.[1] The introduction of heteroatoms (oxygen, nitrogen, sulfur) into the macrocyclic skeleton limits the conformational

freedom and organizes the donor atoms for specific metal binding via coordination bonds. The selective binding of macroheterocycles to specific metals depends on the nature, position and number of heteroatoms in the ring, the ring size, as well as on the presence of functional groups in the ring and in its periphery. Transition metal complexes of macroheterocycles are of particular interest due to their potential catalytic and biochemical activity. Unlike the most common macroheterocycles with hard O- and N-donor atoms, P-containing macrocycles are able to bind soft cations,[6] in particular late transition metals. Despite the high potential of macrocyclic oligophosphines, their use in coordination and supramolecular chemistry or catalysis is quite limited, due to their challenging synthesis and the formation of mixtures of stereoisomers. Numerous synthetic methodologies have been developed for the rational design of macrocyclic phosphines, such as high dilution or template synthesis and – as a relatively novel approach – the covalent self-assembly of macrocycle in dynamic covalent chemistry (DCvC).[7] The covalent self-assembly includes the formation of complicate structures through the generation of dynamic system of molecular entities that able assemble and disassemble due to the reversibility dynamic covalent bonds to give the more termodynamically preferred product.[8-14] Last approach has principally features in comparison of classic synthetic organic chemistry. Most covalent chemistry is irreversible and so occurs under kinetic control while most dynamic covalent chemistry is reversible and so occurs under thermodynamic control. [8-14] The covalent self-assembly proceed at common concentrations of reagents and not required the high dilution or template agents. The slow kinetic of dynamic covalent bond formation usually requires a catalyst to help the system to equilibrate to the thermodynamically stable product on a reasonable time scale.[8-14] The most prominent example and most extensively used dynamic, reversible covalent bond formation since the inception of DCvC is the C–N bond in imines through condensation reaction of an aldehyde with an amine. Dynamic imines have been applied in a remarkable variety of applications, including formation of complex molecular architectures, self-sorting systems, switches and molecular motors.[15] A similar approach has been used for the synthesis of 22-membered P_2N_4 macrocycles containing four imine and two phosphine groups [16, 17] and of 14- and 15-membered P_2N_2 macrocycles with two imine and two phosphine groups,[18,19] where the phosphine groups were included in the starting material and not involved in new bond formation. The

synthesis of phosphorus macrocycles by self-assembly involving dynamic P-C bond formation is quite rare, although many reactions in phosphorus chemistry can be attributed to DCvC. For example, the condensation reaction of isophthaloyl chloride and methyl-bis(trimethylsilyl)phosphane under mild conditions affords (1,10-dimethyl-1,10-diphospha-[3.3]-metacyclophane-2,9,11,18-tetraone in high yield.[20] Formation of a tetraphosphonium macrocycle was observed in the tetramerization of 3-(diphenylphosphino)propanal under acidic conditions.[21] Our previous works clearly demonstrates that the Mannich-like condensation reaction of primary phosphines or secondary bis-phosphines, formaldehyde and primary or secondary amines and bis-amines can be employed for the selective synthesis of a wide range of macrocyclic aminomethylphosphines, namely $[P_2N_2]_2$-cyclophanes, $[P_2N_4]$-cyclophanes, $[P_4N_2]$-cryptand and $[P_4N_2]$-corands.[22-29] Their synthesis, which is accompanied by reversible P-C and C-N bond formation, proceeds with a remarkable stereoselectivity. Thus, in accordance with the main principles of DCvC (reversibility, thermodynamic control, interconversion of molecular components of dynamic system) in the covalent self-assembly of $[P_4N_2]$-corands only one isomer with a preferred configuration of the four endocyclic phosphorus atoms is isolated from the dynamic system containing five possible stereoisomers of $[P_4N_2]$-corands (Fig.1) and $[P_2N]$-corands as products of [1+1] condensations as well as cyclic and acyclic oligomers

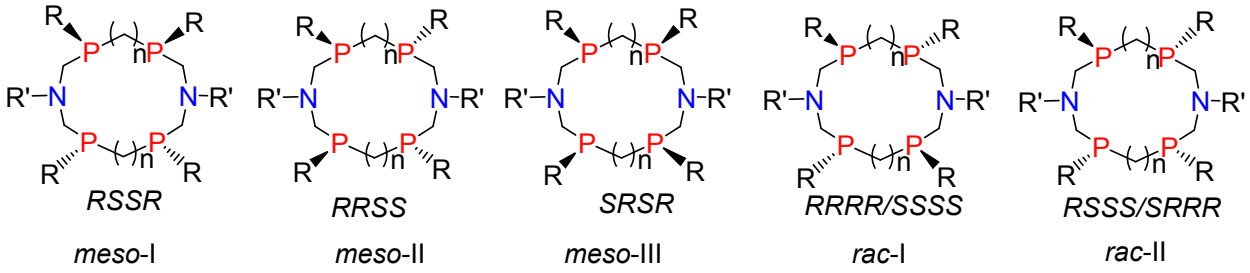


Figure 1. Five possible diastereomers of P_4N_2-macrocycles.

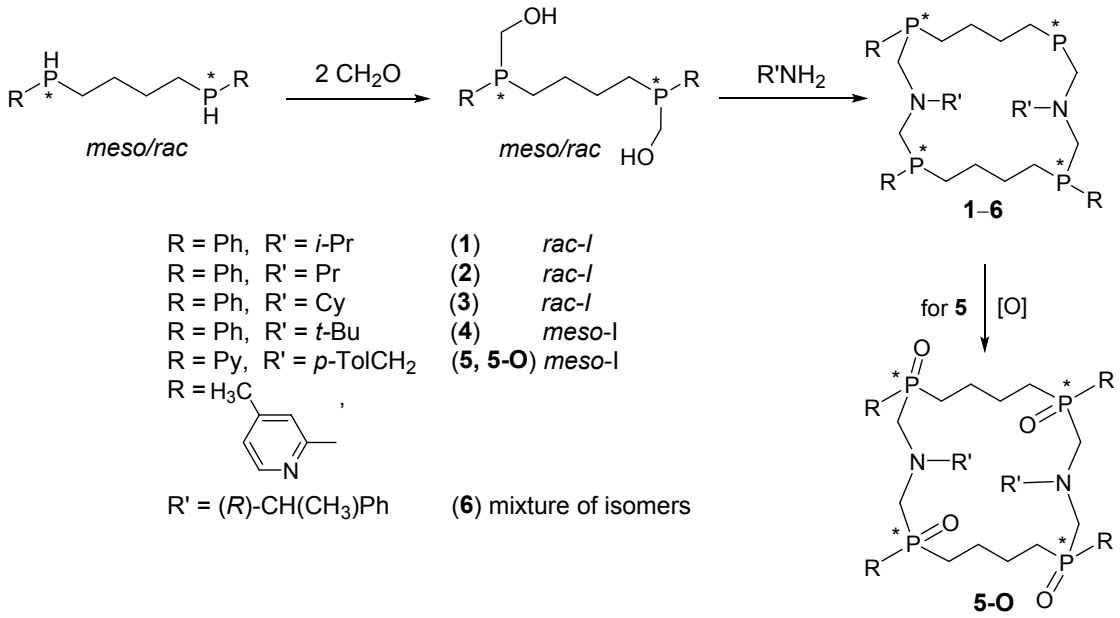
Thus, the 16- and 20- membered macrocycles (where n = 3 and 5 correspondingly) were always isolated as the *meso*-I ($R_PS_PS_PR_P$) isomers[22-24,] but their 14-membered and one 18-membered homologues (where n = 2 and 4 correspondingly) were *rac*-I - $R_PR_PR_PR_P/S_PS_PS_PS_P$ isomers.[22,25-28] Based on these observations, an empirical rule for predicting the configuration of the preferred $[P_4N_2]$-macrocycle on the number of

methylene fragments (even or odd) in the initial bis-phosphine was deduced.[27] Unexpectedly, the *meso*-I isomer of 14-membered P_4N_2 macrocycles was recently obtained from the reaction mixture of 1,2-bis(phenylphosphino)ethane, formaldehyde and primary amine when a different work-up procedure of the reaction mixture was employed, namely crystallization from diethyl ether or ethanol instead of crystallization from DMF.[28] Furthermore, an 18-membered P_4N_2 macrocycle was obtained as *meso*-I isomer from the condensation reaction of 1,4-bis[hydroxymethyl(pyridine-2-yl)phosphino]butane and 4-methylbenzylamine.[29] These compounds were the first exceptions for the abovementioned rule. The behavior of $[P_4N_2]$-corands in solutions appears to be more complex than expected due to the lability of the P-CH_2-N fragment. Thus, the interconversion of isomers for 16-membered P_4N_2 macrocycles and splitting of 14-membered P_4N_2 macrocycles into two 7-membered P_2N macrocycles have been found.[22-28] It turned out that many external factors, in particular temperature, solvent, presence of protons or metal ions, influence these processes.

In order to explore the scope of the covalent self-assembly approach to P_4N_2 macrocycles design and "even/odd" rule in particulary as well as to study the behavior of P_4N_2 macrocycles in solution especially during complex formation, we here report the DCvC of 18-membered P_4N_2 macrocycles and their nickel(II) complexes. We expect that on complexation the most stable complex will be formed and, therefore, the best "fitting" stereoisomer will be selected from the dynamic system.

Results and Discussion

The reaction of 1,4-bis[(hydroxymethyl)(R)phosphino]butane (R = Ph, 2-Py, 4-methylpyridine-2-yl) obtained *in situ* from 1,4-bis[(R)phosphino]butane (R = Ph, 2-Py, 4-methylpyridine-2-yl) and paraformaldehyde as diastereoisomeric mixtures (*rac* and *meso* isomers), with primary alkyl- or benzyl-substituted amines in DMF at 80 °C gave 18-membered 1,10-diaza-3,8,12,17-tetraphosphacyclooctadecanes **1**–**6** (Scheme 1).



Scheme 1. Synthesis of 18-membered P_4N_2 macrocycles **1**–**6**.

Monitoring of the reaction mixtures by $^{31}P\{^1H\}$ NMR spectroscopy indicated that the reactions proceed via the formation of a large number of intermediates and only at the end the main macrocyclic product is formed. It indicates the reversibility of P-C and C-N bonds formation and interconversion of all components of dynamic system and self-correction of reaction which characterize the covalent self-assembly of macrocycle according to DCvC principles. In the final reaction mixtures, several intensive signals in the range of -30 to - 40 ppm were observed which are typical for macrocyclic aminomethylphosphines.[23-29] The intensity of the signals of by-products (acyclic aminomethylphosphines or possible 9-membered cycles as products of [1+1] cyclocondensation reactions in the range of -24 to -28 ppm) was noticeably lower than that of macrocyclic product indicating that the formation of 18-membered macrocycles is more favorable in comparison with other possible products of condensation reaction.

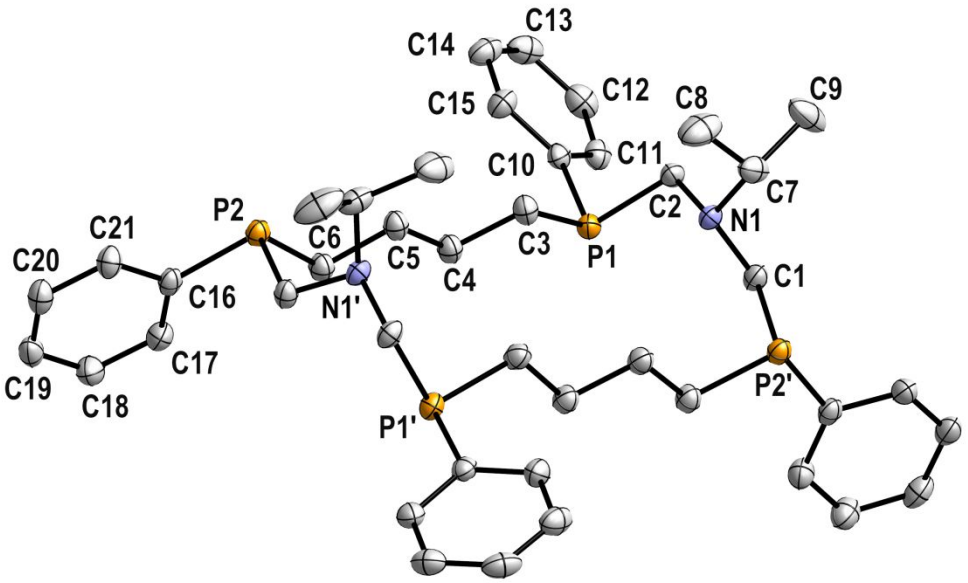
The macrocycles **1**–**5** crystallized from the concentrated reaction mixtures at 0 °C to -10 °C in moderate or good yields of 31 to 61%, whereas all attempts to crystallize the individual product **6** were unsuccessful. The isolated compounds **1**–**5** are air-stable in the solid state and readily soluble in chloroform, dichloromethane and benzene. The elemental analysis, mass spectra and NMR spectroscopy confirmed the structures of macrocycles **1**–**5**. The presence of only one narrow signal at -31.7 to -37.7 ppm in the $^{31}P\{^1H\}$ NMR spectra indicated that only one symmetric diastereoisomer of five possible isomers was crystallized. On the contrary, the $^{31}P\{^1H\}$ NMR spectrum of the viscous oil

of **6** showed a very large number of signals between -29 and -32 ppm indicating the presence of probably all possible stereoisomers. The ^{1}H NMR spectra of compounds **1**–**5** are similar to those of the previously reported 14- and 16-membered macrocycles.[22-27] The protons of the P-$(CH_2)_4$-P fragment give two or three multiplets in the range of 1.5 to 1.9 and 1.9 to 2.3 ppm. The methylene protons of the -PCH_2N- fragments of **1**–**3** are observed as two multiplets (doublets or doublets of doublets) at 2.55 to 2.70 ppm ($^{2}J_{HH}$ = 12.4 to 13.2 Hz, $^{2}J_{PH}$ = 10 to 17.2 Hz) and 3.47 to 3.63 ppm ($^{2}J_{HH}$ = 12.4 to 13.2 Hz, $^{2}J_{PH}$ = 0 to 6.8 Hz). The similar patterns indicate analogous structures of these fragments; thus, the isolated macrocycles **1**–**3** are probably the same diastereomer. In the case of compounds **4** and **5**, the corresponding signals of the butylene fragment are also observed as two multiplets, but the doublet or doublet of doublets of the -PCH_2N- fragments undergo a noticeable low-field shift up to 3.30 to 3.33 ppm. The coupling constants also differ from those of **1**–**3** (Table 1), indicating a different geometry of the P-CH_2-N fragments and thus another diastereoisomer of these 18-membered macrocycles.

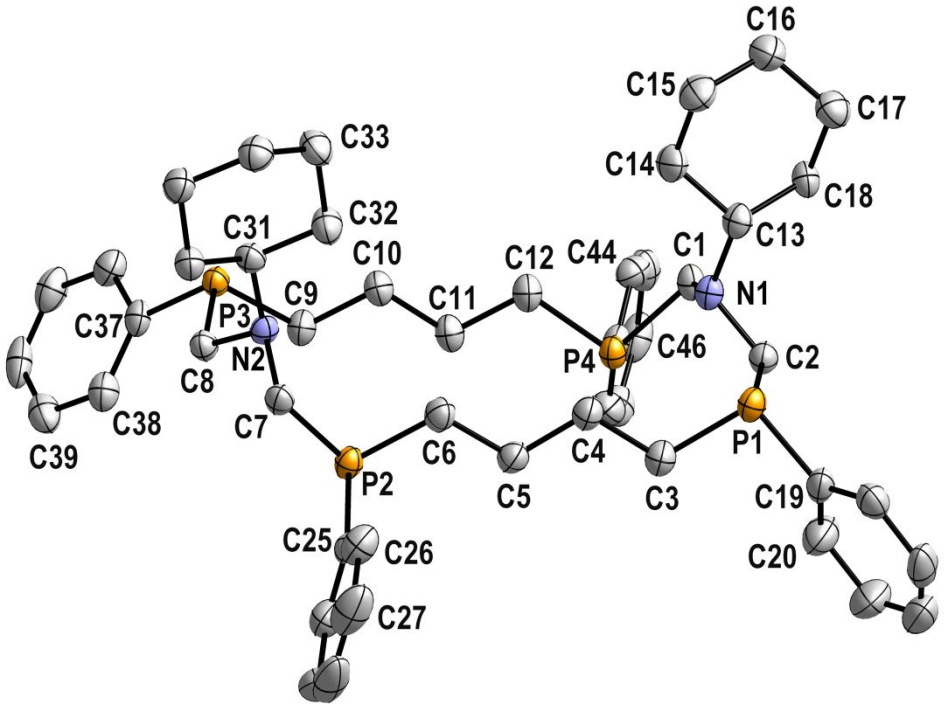
Table 1. Yields and selected NMR spectroscopic data of the macrocycles **1**–**5**.

Compound	R	R'	Yield %	$\delta_{P,}$ ppm	P-CH_A-N, δ_H [ppm], ($^{2}J_{HH,}$ $^{2}J_{PH}$ in Hz)	P-CH_B-N, δ_H [ppm], ($^{2}J_{HH,}$ $^{2}J_{PH}$ in Hz)
1	Ph	Pr^i	38	-36.2	2.55 (13.2; 16.0)	3.47 (13.2; 0)
2	Ph	Pr	33	-37.7	2.69 (12.6; 10.0)	3.65 (12.6; 0)
3	Ph	Cy	39	-35.8	2.70 (12.4; 17.2)	3.53 (12.4; 6.8)
4	Ph	Bu^t	35	-36.2	3.30 (14.2; 0)	3.74 (14.2; 4.0)
5	Py	-CH_2Tol-*p*	61	-31.7	3.33 (13.0; 7.1)	4.00 (13.0; 2.0)

These assumptions were confirmed by X-ray structure analysis of macrocycles **1**, **3** and **4**. As predicted by the even/odd rule,[27] macrocycles **1** and **3** are the $R_PR_PR_PR_P/S_PS_PS_PS_P$ isomers of the corresponding 1,10-diaza-3,8,12,17-tetraphosphacyclooctadecanes (Fig. 2).



a)



b)

Fig. 2. Molecular structures of macrocycles **1** (a) and **3** (b). Only one of the two isomers ($R_PR_PR_PR_P/S_PS_PS_PS_P$), namely the $R_PR_PR_PR_P$ isomer, is shown. Hydrogen atoms are omitted for clarity. Molecule **1** on a special position on axe 2. Displacement ellipsoids are drawn at the 50% probability level.

The substituents on phosphorus atoms are in equatorial position and the lone pair of electrons at the phosphorus atoms have an *anti-anti-anti* orientation. The butylene fragments including phosphorus atoms have *zig-zag* conformation so that the phosphorus atoms are *trans*-oriented. *Zig-zag* like alkylene chains appear to be a common feature of 14-, 16-, 18- and 20-membered macrocyclic aminomethylphosphines. A *zig-zag*

conformation provides the minimal number of eclipsed conformations of the CH_2 fragments, which is probably the main reason for the predominance of the larger macrocycles compared to smaller rings. The P-CH_2-N-CH_2-P fragments are twisted and substituents at nitrogen atoms are in axial positions and *syn*-oriented. The lone pair of electrons at the nitrogen atoms are directed towards the cavity of the macrocycle. The overall structure of the macrocycles in **1** and **3** is similar to that of the $R_PR_PR_PR_P/S_PS_PS_PS_P$ isomers of 14-membered 1,8-diaza-3,6,10,13-tetraphosphacyclotetradecanes and differs mainly in the longer hydrocarbon bridge which is also reflected in a larger P···P distance (6.954 to 6.994 Å for 18- and 4.477 Å for 14-membered macrocycles)[26] whereas the P···P distance between phosphorus atoms bridged by the CH_2–N–CH_2 fragment have similar values (4.527 to 4.695 Å for 18- and 4.738 Å for 14-membered macrocycles)[26].

Compound **4** whose NMR spectroscopy data differed from that of macrocycles **1**–**3** indeed crystallized as the $R_PS_PS_PR_P$ isomer of the corresponding 1,10-diaza-3,8,12,17-tetraphosphacyclooctadecane (Fig. 3) and adopted another conformation than macrocycles **1** and **3**. Moreover, the conformation of **4** is essentially different from that of the *meso*-I isomer of 16-membered 1,9-diaza-3,7,11,15-tetraphosphacyclohexadecanes with a *zig-zag*-type propylene chains between the phosphorus atoms,[23,24] but is very similar to the conformation of the $R_PS_PS_PR_P$ isomer of 14-membered 1,8-diaza-3,6,10,13-tetraphosphacyclotetradecane[28]. Both fragments P-CH_2-N-CH_2-P and P-CH_2-CH_2-CH_2-CH_2-P in **4** have twisted conformations, in which all heteroatoms are located in the same plane and all exocyclic substituents are in equatorial positions. The lone pairs of electrons at the nitrogen atoms have *anti* orientation whereas the lone pairs of electrons at phosphorus have a mutual *syn-anti-syn* arrangement. The P···P distances between phosphorus atoms bridged by butylene chains (5.834 to 6.126 Å) or the CH_2–N–CH_2 fragment are shorter in comparison with the corresponding distances of the $R_PR_PR_PR_P/S_PS_PS_PS_P$ isomers of macrocycles **1** and **3** (6.954 to 6.994 Å and 4.524 to 4.694 Å). At the same time, the diagonal P···P distances are longer (8.16 Å in the $R_PS_PS_PR_P$ isomer compared to 6.95 Å for $R_PR_PR_PR_P/S_PS_PS_PS_P$-**1** and -**3**)

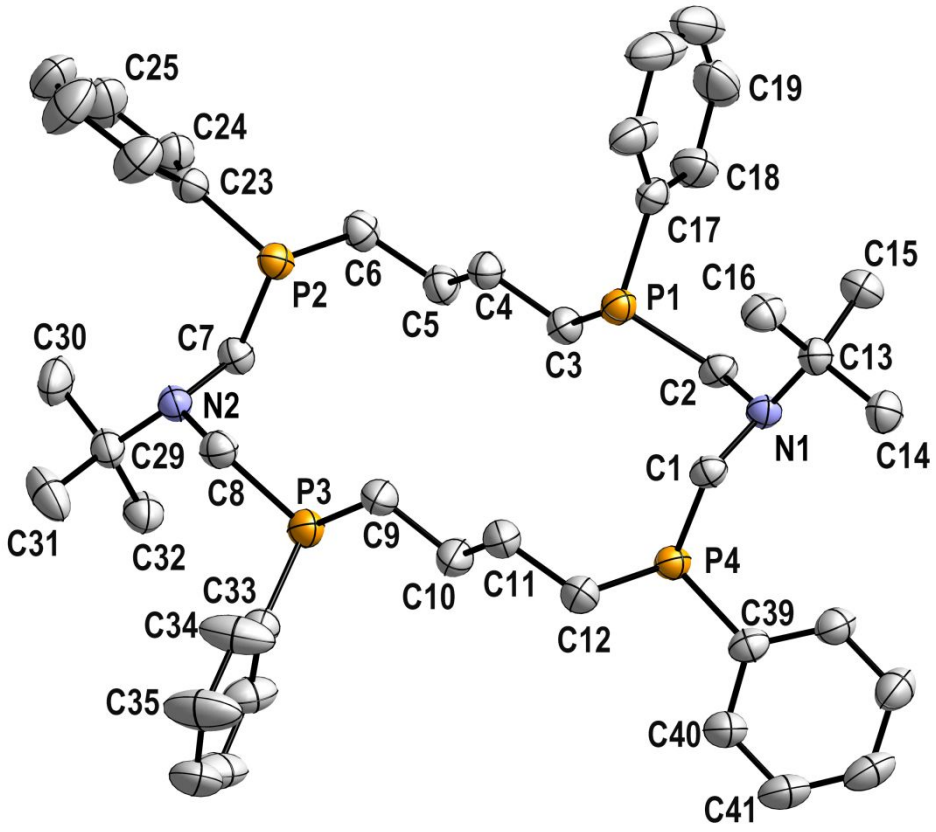


Fig. 3. Molecular structure of **4** ($R_PS_PS_PR_P$ isomer). Hydrogen atoms are omitted for clarity. Displacement ellipsoids are drawn at the 50% probability level.

The similar NMR spectra observed for macrocycles **4** and **5** allow the conclusion that **5** also forms the *meso*-I isomer. Furthermore, confirmation has been obtained with the molecular structure of the corresponding tetrakisphosphine tetraoxide **5-O**, as oxidation of phosphines (including the macrocycles with several phosphine centers) proceeds with retention of the configuration of the phosphorus atoms.[30] The tetraoxide **5-O** was obtained on crystallizing **5** without protection from air. The $^{31}P\{^1H\}$ NMR spectrum of **5-O** showed one narrow singlet at 39.6 ppm indicating full oxidation of all four phosphorus atoms. The ^1H NMR spectrum of **5-O** also indicates a symmetrical structure. The methylene protons of the P-CH_2-N fragments are observed as two doublets of doublets at 2.92 and 4.03 ppm; the high-field position of the first signal is typical for macrocyclic aminomethylphosphines.

The X-ray structure analysis confirmed the $R_PS_PS_PR_P$ isomer of the 18-membered 3,8,12,17-tetraoxo-1,10-diaza-3,8,12,17-tetraphosphacyclooctadecane **5-O** (Fig. 4).

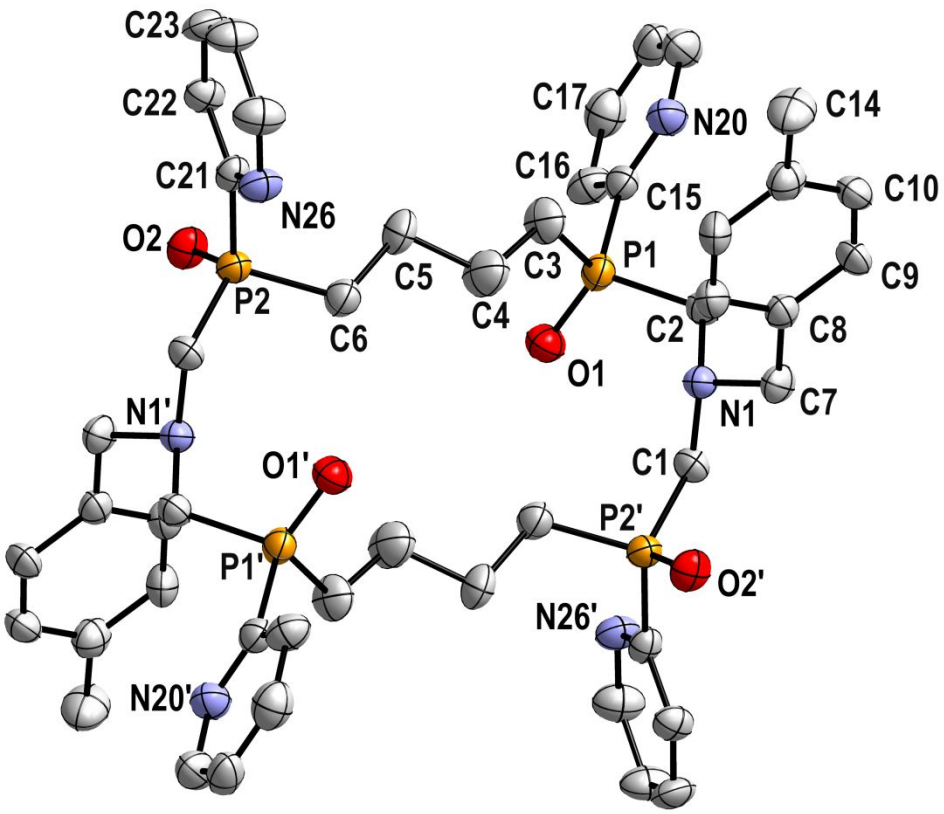
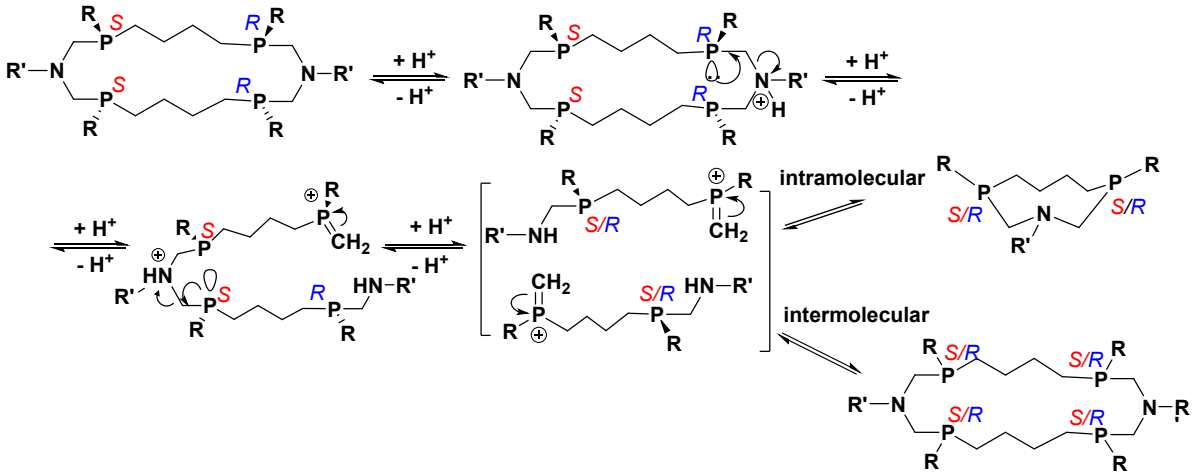


Fig. 4 Molecular structure of tetrakisphosphine tetraoxide **5-O**. Hydrogen atoms and solvate molecules are omitted for clarity. Displacement ellipsoids are drawn at the 20% probability level.

The conformation of the macrocycle **5-O** essentially differs from the conformations of unoxidized P_4N_2 macrocycles. The main difference is the spatial arrangement of the *zig-zag* butylene fragments bridging the phosphorus atoms P1 (P1') and P2 (P2'): all carbon atoms (C3C4C5C6 and C3'C4'C5'C6' are located in one plane. The phosphorus atoms P1 and P1', P2 and P2', and the nitrogen atoms N1 and N1' occupy mutual *trans* positions relative to this plane. Exocyclic substituents on the phosphorus atoms are in equatorial position, and the oxygen atoms have a mutual *syn-anti-syn* arrangement corresponding to the $R_PS_PS_PR_P$ isomer. The P-CH_2-N-CH_2-P fragments adopt *twist* conformations so that the nitrogen atoms and their lone pairs of electrons are directed towards the macrocyclic cavity. The P-O bond lengths (1.494(6) to 1.500(7) Å) are typical for phosphine oxides.

As mentioned above, the macrocyclic aminomethylphosphines demonstrate dynamic behavior in solution due to the labile P-CH_2-N fragment. There are processes of isomers interconversion and partial splitting of 16-membered P_4N_2 macrocycles into two 8-

membered P_2N cycles[23] and practically full splitting of 14-membered P_4N_2 macrocycles into two 7-membered P_2N cycles[25, 26]. According to $^{31}P\{H\}$ NMR spectroscopic studies, in solution the pure stereoisomers of the 18-membered P_4N_2 macrocycles **1**–**5** form a dynamic system of cyclic aminomethylphosphines where the initial isomer (*rac*-I for compounds **1**–**3**, *meso*-I for compounds **4**, **5**) prevails (Fig. S25-S29). The second main signal in the $^{31}P\{^1H\}$ spectra of macrocycles **1**–**5** in the region from -31 to -37 ppm belong to another stereoisomer of 18-membered P_4N_2 macrocycle (the most probably it is *meso*-I for **1**–**3**, and *rac*-I for compounds **4**, **5**). The number signals with low intensity indicates the possible formation of other cyclic aminomethylphosphines. However, in contrast to the $^{31}P\{^1H\}$ spectra of 14- and 16-membered P_4N_2 macrocycles the intensity of signals of possible 9-membered cycles in the spectra of 18-membered macrocycles is very low that indicates the predominant process of stereoisomerization whereas the splitting into 9-membered cycles is negligible. The mechanism of transformation of macrocyclic aminomethylphosphines has been proposed recently.[23] Process includes the proton-induced rupture of endocyclic C–N bond and formation of a methylenephosphonium intermediate and the following intra- or intermolecular nucleophilic attack of the nitrogen atom at the carbon atom of methylenephosphonium intermediate which should result in formation of the corresponding 1-aza-3,8-diphosphacyclononanes or 18-membered macrocycles with all possible configurations at phosphorus (Scheme 2).

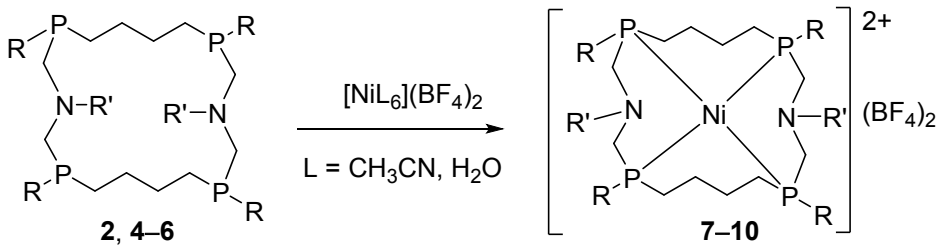


Scheme 2. Proposed mechanism illustrating transformations of $R_PS_PS_PR_P$ isomer of 1,10-diaza-3,8,12,17-tetraphosphacyclooctadecane.

The predominantly stereoizomerisation of 18-membred macrocycles testify the intermolecular way of nucleophilic attack for 18-membered cycles which caused probably by longer chain between reactive centres then for 14- and 16-membered cycles.

A key advantage of DCvC is the ability of dynamic systems to response to external interventions. For the dynamic reaction a number of external factors, such as temperature, concentration, pressure, and impurities, can have a dramatic effect upon the equilibrium and so change the product distribution. This adjustable set of parameters opens up the attractive possibility of being able to design and make molecules that can adapt to their surroundings.[8] Recently, we demonstrated that complexation of copper(I) by P_4N_2 macrocycles results in retention or in stereoisomerisation of the P_4N_2 ligand depending on the geometry of the initial tetrakisphosphine. Namely, the $R_PR_PR_PR_P/S_PS_PS_PS_P$ isomers of 14-membered P_4N_2 macrocycles form very stable tetrahedral cationic mononuclear complex,[31] whereas the $R_PS_PS_PR_P$ isomer of 14-membered P_4N_2 macrocycles gives dicopper bis-P,P-chelate complexes[28] independent of the stoichiometry employed. In both cases, the tetrakisphosphine ligands retain their configuration. Both $R_PR_PR_PR_P/S_PS_PS_PS_P$ and $R_PS_PS_PR_P$ isomers of 16-, 18- and 20-membered P_4N_2 macrocycles give dicopper bis-P,P-chelate complexes with the $R_PR_PS_PS_P$ isomer of the P_4N_2 ligand.[31] Apparently, in solution reorganization of the orientation of the lone pairs of electrons at the phosphorus atoms to allow formation of the thermodynamically most stable transition metal complex is a very important feature of tetrakisphosphine ligand. Here, we report the reaction of various isomers of 18-membered P_4N_2 macrocycles with nickel(II) tetrafluoroborate as precursor of tetrakisphosphine complexes with square-planar geometry.

The reactions of the pure $R_PR_PR_PR_P/S_PS_PS_PS_P$ isomer of **2**, the $R_PS_PS_PR_P$ isomers of **4** and **5** and even a mixture of isomers of **6** with one equivalent of hexaaquanickel(II) or hexaacetonitrilenickel(II) tetrafluoroborate in acetonitrile or THF proceeded through the formation of a variety of unidentified intermediate complexes according to $^{31}P\{^1H\}$ NMR monitoring, but finally led to the formation of mononuclear cationic complexes **7**–**10** only (Scheme 3) which were isolated in 38 to 76 % yield.



R = Ph, R' = Pr (**2, 7**)
R = Ph, R' = Bu^t (**4, 8**)
R = Py, R' = CH_2Tol^p (**5, 9**)
R = H_3C , R' = (*R*)-$CH(CH_3)Ph$ (**6, 10**)

Scheme 3. Synthesis of complexes **7** – **10**

The $^{31}P\{^1H\}$ spectra of complexes **7**–**10** showed one narrow signal in the range of -10 to 10 ppm indicative of a symmetrical structure. A noticeable difference in the chemical shifts between P-phenyl-substituted complexes **7** and **8** (ca. -6 ppm) and P-pyridyl-substituted complexes **9** and **10** (ca. 8 to 11 ppm) was observed. The solubility of P-phenyl- and P-pyridyl-substituted complexes was also different. Complexes **7** and **8** were soluble in most organic solvents (acetonitrile, dichloromethane etc.) whereas complexes **9** and **10** were satisfactorily soluble only in DMF. The ^1H NMR spectra of **7**, **8** and **9**, **10** also differed. For **7**–**10**, the two halves of the macrocycle are equivalent and the protons of the P-CH_2-N fragments are observed as two doublets at 2.86 and 3.17 ppm for **7**, at 2.90 and 3.15 ppm for **8**, and at lower field for complexes **9** and **10**, namely at 3.26 and 3.34 ppm for **9**, at 3.24 and 3.30 ppm for **10**. The reason for the observed different physical and spectroscopic properties was established from the X-ray crystal structure data of complexes **7, 9** and **10** (Figs. 5 to 7).

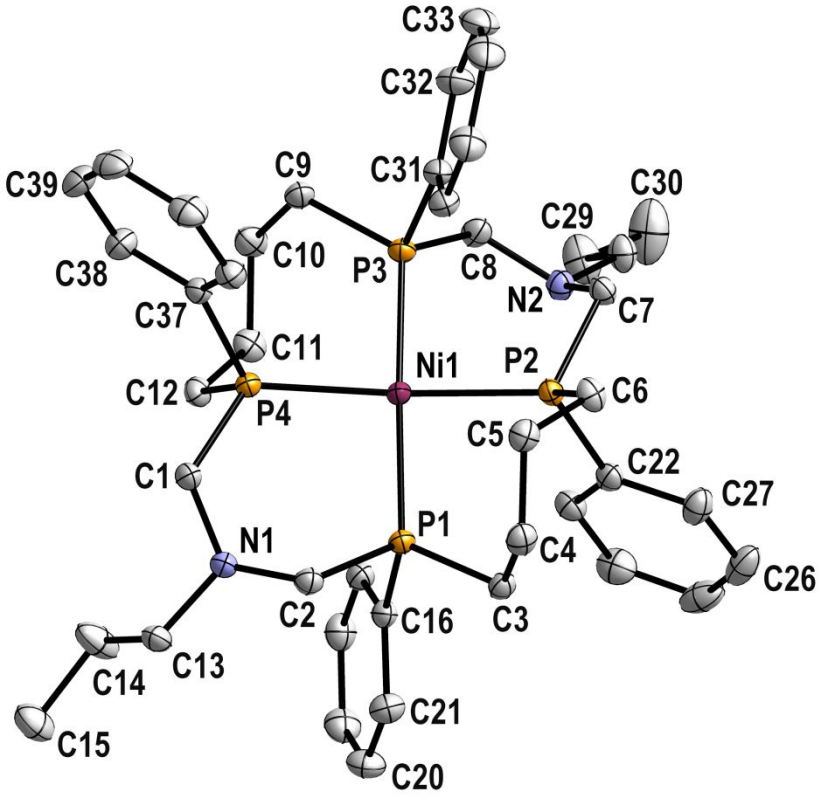


Fig. 5. Molecular structure of the cation in **7**. Hydrogen atoms are omitted for clarity. Anions are not shown. Displacement ellipsoids are drawn at the 50% probability level.

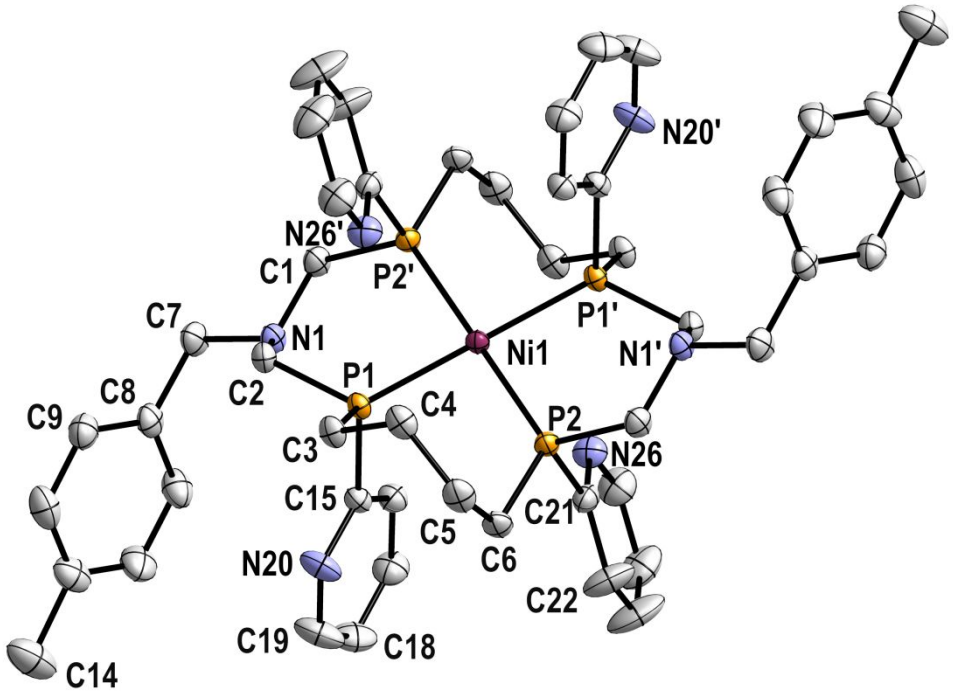


Fig. 6. Molecular structure of the cation in **9** (the molecule is located on an inversion center). Hydrogen atoms are omitted for clarity. The second independent cation and the anions are not shown. Displacement ellipsoids are drawn at the 20% probability level.

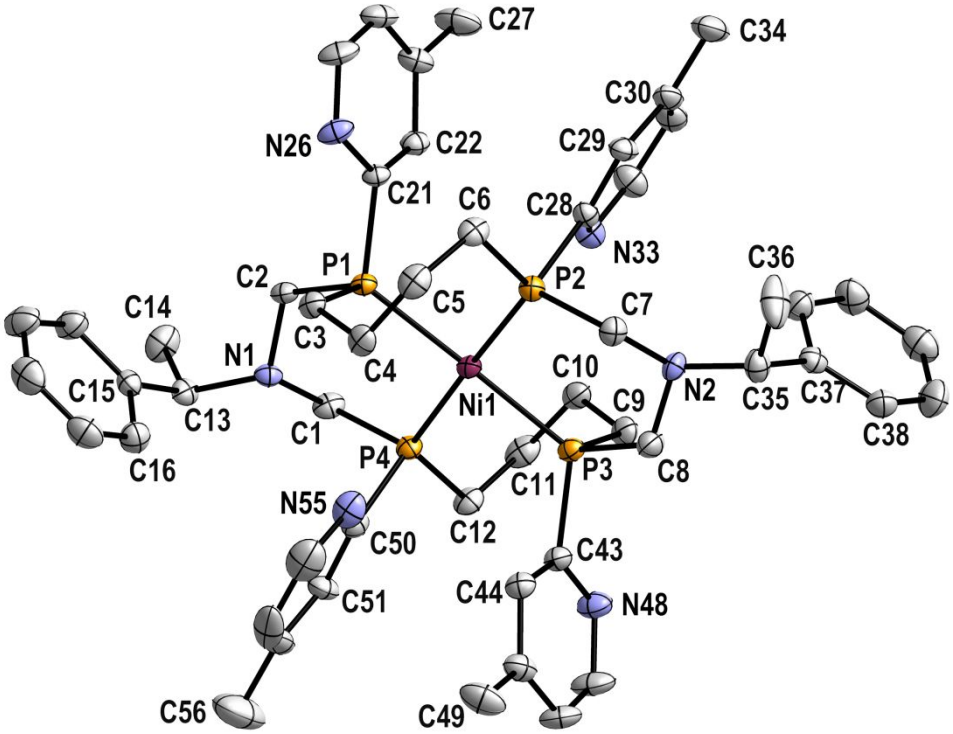


Fig. 7. Molecular structure of the cation in **10**. Hydrogen atoms are omitted for clarity. Anions are not shown. Displacement ellipsoids are drawn at the 20% probability level.

Compounds **7**, **9** and **10** are cationic mononuclear complexes. The nickel(II) has an almost ideal square-planar environment (**7, 9** and **10**, sum of bond angles is 360.58(2)°, 360° and 359.99(8)°, respectively, in **9**, Ni1 is located on an inversion center) formed by the four phosphorus atoms of the macrocyclic ligand. The average Ni-P bond length (2.194 to 2.236 Å) in agreement with the usual values found in square-planar nickel(II) complexes.[32,33] The P-Ni-P bite angles are 87.23(8) to 92.58(2)°. In all complexes, the $R_PS_PS_PR_P$ isomers of the ligands are present. The exocyclic substituents at the phosphorus atoms are in a *syn-anti-syn* arrangement. Four chelate rings – two six- and two seven-membered rings – are formed as a result of nickel(II) coordination. The six-membered rings have a *half-chair* conformation, the seven-membered rings a *twist-chair* conformation. The position of the aminomethyl fragments relative to the P_4Ni plane are different for complex **7** and complexes **9** and **10**. In **7**, both amino groups are located on the same side relative to the P_4Ni plane, whereas in complexes **9** and **10**, they are located on opposite sides of the plane. The two nitrogen atoms of the ligands have a pyramidal coordination (sum of bond angles is 336.0(2) to 341.1(1)°); their lone pairs of electrons

are directed towards the metal center without coordination, but in close proximity (Ni···N 3.589(2) to 3.790(7) Å).

Conclusions

We have demonstrated that the principles of DCvC (reversibility of reactions, dynamic systems, self-assembly) are also applicable for the stereoselective synthesis of 18-membered P_4N_2 macrocycles as individual *rac*-I ($R_PR_PR_PR_P/S_PS_PS_PS_P$) or *meso*-I ($R_PS_PS_PR_P$) isomers, *via* Mannich-like condensation reactions of 1,4-bis(organylphosphino)butane, formaldehyde and primary amines. This approach can be applied for the synthesis of a large variety of P_4N_2 macrocycles with variably ring sizes and substituents at the heteroatoms. The obtained 18-membered P_4N_2 macrocycles form square-planar nickel(II) complexes as meso-I isomers exclusively, in spite of the configuration of the initial ligand, indicating their ability to stereoisomerize in the course of the complexation of nickel(II) salts to give the most stable complex. This fact and the recently described stereoselective formation of tetrahedral mononuclear copper(I) complexes with exclusively the *rac*-I $R_PR_PR_PR_P/S_PS_PS_PS_P$ isomer of P_4N_2 macrocycles and formation of dicopper bis-P,P-chelate complexes with only the *meso*-II $R_PR_PS_PS_P$ isomer of the P_4N_2 macrocycles suggest that macrocylic aminomethylphosphines behave like "smart" ligands that can adjust to the requirements of the metal ion *via* the described dynamic systems, thus allowing the quantitative formation of the thermodynamically preferred complex with only one stereoisomer as ligand.

EXPERIMENTAL SECTION

General Methods. All reactions and manipulations with phosphines **1**–**6** were carried out under a dry argon atmosphere using standard vacuum-line and Schlenk techniques. All manipulations with complexes **7**–**10** were carried out under normal conditions without inert atmosphere. Solvents were purified, dried, deoxygenated, and distilled before use. ^{1}H NMR spectra were recorded on a Bruker Avance DRX 400 (400 MHz) and Bruker Avance-600 (600 MHz) spectrometer. Chemical shifts are reported in parts per million from tetramethylsilane with the solvents resonances as internal standards. Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br = broad, m = multiplet), coupling constants (Hertz), integration, and

assignment. ^{13}C NMR spectra were recorded on a Bruker Avance DRX 400 spectrometer (100.5 MHz) with complete proton decoupling. Chemical shifts are reported in parts per million with the solvents as internal standards. ^{31}P NMR spectra were recorded on a Bruker Avance DRX 400 (162 MHz) and Bruker Avance-600 (242 MHz) spectrometer, and chemical shifts are reported relative to external 85% H_3PO_4. MALDI-TOF mass spectrometry was performed using an Ultraflex III TOF/TOF (Bruker Daltonics, Germany) spectrometer. The FlexAnalysis 3.0 (Bruker Daltonics) program was used to process the mass spectrometry data. ESI_{pos} mass spectrometry was performed using an AmazonX (Bruker Daltonic GmbH, Bremen, Germany) spectrometer at a capillary voltage of 3500 V. The DataAnalysis 4.0 (Bruker Daltonic GmbH, Bremen, Germany) program was used to process the mass spectrometry data. The mass spectra are reported as m/z values. Determination of the CHN content was carried out on a CHNS analyzer EuroEA3028-HT-OM (Eurovector SpA, Italy). Determination of the phosphorus content was provided by combustion in an oxygen stream.

1,4-[Bis(pyridine-2'-yl)phosphino]butane and 1,4-bis[(4'-methyl-pyridine-2'-yl)phosphino]butane were prepared by the reported method.[34] 1,4-Bis(phenylphosphino)butane was prepared by an improved method used for the synthesis of other secondary bis-phosphines.[35]

1,4-Bis(phenylphosphino)butane. A solution of 1,4-bis(diphenylphosphino)butane (38.3 g, 0.09 mol) in dry degassed THF (150 mL) was added dropwise to lithium chips (6.2 g, 0.56 mol) in dry degassed THF (150 mL) at 0 °C for 4 h and the reaction mixture was stirred under reflux for 2 h. The hot reaction mixture was filtered to remove the unreacted lithium and the filtrate was cooled to 0 °C. A THF/water mixture (4:1) (25 mL) was added dropwise to this deep red filtrate. Decolorization and formation of a white precipitate were observed. THF was removed in vacuo and the residual aqueous solution was extracted with ethyl ether (3 × 80 mL). The combined organic fractions were dried with $MgSO_4$ overnight and the ethyl ether was removed by distillation under atmospheric pressure. The residue was heated to 150 °C on the oil bath at 0.01 torr for 30 min to remove all volatiles. The residual viscous oil was 1,4-bis(phenylphosphino)butane (17.3 g, 70 %). ^1H NMR (400 MHz, $CDCl_3$) δ = 7.41 – 7.49 (m, 4H), 7.25 – 7.29 (m, 6H), 4.06 (ddd, $^1J_{PH}$ = 209.8 Hz, $^2J_{PH}$ = 7.1 Hz, $^2J_{PH}$ = 6.8 Hz, 2H), 1.74 – 1.85 (m, 2H), 1.65 – 1.71 (m, 2H), 1.42 – 1.57 (m, 4H); $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$) δ -52.16, -52.13.

General procedure for the synthesis of 1,10-diaza-3,8,12,17-tetraphosphacycloocta-decanes (1–5). A solution of 1,4-bis[(hydroxymethyl)arylphosphino]butane (1 mmol) (obtained in situ by heating a mixture of 1,4-bis(arylphosphino)butane (1 mmol) and paraformaldehyde (2 mmol) at 100-110 °C on the oil bath until homogenization occurred) and the primary amine (1 mmol) in DMF (10 mL) was stirred at 80 °C on the oil bath for 7 to 24 h. The reaction mixture was cooled and concentrated in vacuo to 1/4 to 1/6 of the initial volume. The residue was crystallized at 0 to -10 °C. The crystalline precipitate was filtered off, washed with ethanol or ethyl ether and dried for 4 to 5 h at 0.01 torr.

1,10-Diisopropyl-3,8,12,17-(*RRRR/SSSS*)-tetraphenyl-1,10-diaza-3,8,12,17-tetraphosphacyclooctadecane (1). Reaction time 24 h. Yield of **1**: 0.136 g (38 %); white solid, mp 98–100 °C. ^{1}H NMR (400 MHz, C_6D_6) δ 7.49 – 7.57 (m, 8H), 7.10 – 7.24 (m, 12H), 3.91 (m, 2H), 3.47 (br.d, $^{2}J_{HH}$ = 13.2 Hz, 4H), 2.55 (dd, $^{2}J_{HH}$ = 13.2 Hz, $^{2}J_{PH}$ = 16.0 Hz, 4H), 2.14 – 2.25 (m, 4H), 1.89 – 1.92 (m, 4H), 1.67 – 1.77 (m, 8H), 1.08 (d, $^{3}J_{HH}$ = 6.6 Hz, 6H), 0.70 (d, $^{3}J_{HH}$ = 6.6 Hz, 6H); ^{31}P{^{1}H} NMR (162 MHz, C_6D_6) δ -36.2; ^{13}C{^{1}H} NMR (100 MHz, C_6D_6) δ 139.2 (d, $^{1}J_{CP}$ = 14.2 Hz), 133.5 (d, $^{2}J_{CP}$ = 19.5 Hz), 129.3 (s), 129.0 (d, $^{3}J_{CP}$ = 5.8 Hz), 55.7 (d, $^{1}J_{CP}$ = 6.5 Hz), 50.5 (t, $^{3}J_{CP}$ = 23.7 Hz), 30.2 (dd, $^{1}J_{CP} \approx {}^{4}J_{CP} \approx$ 23.7 Hz), 29.1 (d, $^{2}J_{CP}$ = 14.3 Hz), 22.2 (s), 12.7 (s); MALDI MS *m/z* 778 $[M + 4O]^+$. Anal. calc. for $C_{42}H_{58}N_2P_4$ [714.82] C 70.57, H 8.18, N 3.92, P 17.33 %, found: C 70.67, H 8.24, N 3.69, P 17.42 %.

1,10-Dipropyl-3,8,12,17-(*RRRR/SSSS*)-tetraphenyl-1,10-diaza**-3,8,12,17-tetraphosphacyclooctadecane (2).** Reaction time 10 h. Yield of **2**: 0.118 g (33 %); white solid, mp 116–118 °C. ^{1}H NMR (400 MHz, C_6D_6) δ 7.52 – 7.59 (m, 8H), 7.10 – 7.16 (m, 12H), 3.65 (br.d, $^{2}J_{HH}$ = 12.6 Hz, 4H), 2.98 – 3.18 (m, 2H), 2.69 (dd, $^{2}J_{HH}$ = 12.6 Hz, $^{2}J_{PH}$ = 10.0 Hz, 4H), 2.32 – 2.39 (m, 2H), 2.02 – 2.09 (m, 4H), 1.74 – 1.83 (m, 12H), 1.35 – 1.44 (m, 4H), 0.85 (t, $^{3}J_{HH}$ = 7.2 Hz, 6H); ^{31}P{^{1}H} NMR (162 MHz, C_6D_6) δ -37.7; ^{13}C{^{1}H} NMR (100 MHz, C_6D_6) δ 139.5 (d, $^{1}J_{CP}$ = 15.8 Hz), 133.1 (d, $^{2}J_{CP}$ = 19.0 Hz), 128.8 (s), 128.7 (d, $^{3}J_{CP}$ = 7.2 Hz), 59.8 (d, $^{1}J_{CP}$ = 10.6 Hz), 59.5 (t, $^{3}J_{CP}$ = 8.0 Hz), 28.4 (dd, $^{1}J_{CP}$ = 15.6, $^{4}J_{CP}$ = 12.1 Hz), 28.1 (d, $^{2}J_{CP}$ = 13.4 Hz), 20.6 (s), 12.0 (s). ESI_{pos} MS *m/z* 778 $[M + 4O - H]^+$. Anal. calc. for $C_{42}H_{58}N_2P_4$ [714.82] C 70.57, H 8.18, N 3.92, P 17.33 %, found: C 70.70, H 8.28, N 3.82, P 17.35 %.

1,10-Di(cyclohexyl)-3,8,12,17-(*RRRR/SSSS*)-tetraphenyl-1,10-diaza-3,8,12,17-tetraphosphacyclooctadecane (3). Reaction time 7 h. Yield of **3**: 0.155 g (39 %); white solid, mp 129–132 °C. ^{1}H NMR (400 MHz, C_6D_6) δ 7.55 – 7.65 (m, 8H), 7.10 – 7.18 (m, 12H), 3.53 (dd, $^{2}J_{HH}$ = 12.6 Hz, $^{2}J_{PH}$ = 6.6 Hz, 4H), 3.42 – 3.50 (m, 2H), 2.70 (dd, $^{2}J_{HH}$ = 12.6 Hz, $^{2}J_{PH}$ = 17.4 Hz, 4H), 2.23 (ddd, $^{2}J_{HH} \approx {}^{2}J_{PH} \approx$ 12.4 Hz, $^{2}J_{PH}$ = 4.2 Hz, 4H), 1.81 – 1.95 (m, 8H), 1.70 – 1.78 (m, 6H), 1.64 (d, $^{2}J_{HH}$ = 13.2 Hz, 4H), 1.54 (d, $^{2}J_{HH}$ = 13.2 Hz, 4H), 1.29 – 1.40 (m, 4H), 1.07 – 1.19 (m, 2H), 0.92 – 1.02 (m, 2H), 0.75 – 0.84 (m, 2H); ^{31}P{^{1}H} NMR (162 MHz, C_6D_6) δ -35.8; ^{13}C{^{1}H} NMR (100 MHz, C_6D_6) δ 139.0 (d, $^{1}J_{CP}$ = 14.6 Hz, *i*-C_6H_5), 133.2 (d, $^{2}J_{CP}$ = 27.9 Hz, *o*-C_6H_5), 128.9 (d, $^{3}J_{CP}$ = 12.6 Hz), 128.7 (s), 59.5 (s), 56.1 (d, $^{1}J_{CP}$ = 5.9 Hz), 32.7 (s); 29.8 (dd, $^{1}J_{CP} \approx {}^{4}J_{CP} \approx$ 15.5 Hz), 28.7 (d, $^{2}J_{CP}$ = 14.6 Hz), 26.8 (s), 26.2 (s). ESI_{pos} MS *m/z* 873 $[M + O + K + Na]^{+}$. Anal. calc. for $C_{48}H_{66}N_2P_4$ [794.95] C 72.52, H 8.37, N 3.52, P 15.58 %, found: C 72.67, H 8.38, N 3.76, P 15.85 %.

1,10-Di(*tert*-butyl)-3,8,12,17-(*RSSR*)-tetraphenyl-1,10-diaza-3,8,12,17-tetraphosphacyclooctadecane (4). Reaction time 24 h. Yield of **4**: 0.130 g (35 %); white solid, mp 130–132 °C. ^{1}H NMR (400 MHz, C_6D_6) δ 7.35 – 7.40 (m, 8H), 6.84 – 6.97 (m, 12H), 3.74 (ddd, $^{2}J_{HH}$ = 13.9 Hz, $^{2}J_{PH} \approx {}^{4}J_{HH} \approx$ 4.1 Hz, 4H), 3.30 (dd, $^{2}J_{HH}$ = 13.9 Hz, $^{2}J_{PH}$ = 2.2 Hz, 4H), 1.91 – 1.98 (m, 4H), 1.71 – 1.79 (m, 12H), 0.92 (s, 18H); ^{31}P{^{1}H} NMR (162 MHz, C_6D_6) δ -36.1; ^{13}C{^{1}H} NMR (100 MHz, C_6D_6) δ 140.3 (d, $^{1}J_{CP}$ = 17.9 Hz), 133.6 (d, $^{2}J_{CP}$ = 18.9 Hz), 129.0 (s), 128.6 (d, $^{3}J_{CP}$ = 6.5 Hz), 55.2 (br.s), 54.4 (t, $^{3}J_{CP}$ = 9.1 Hz), 28.6 (dd, $^{1}J_{CP} \approx {}^{4}J_{CP} \approx$ 14.6 Hz), 27.9 (s), 27.8 (d, $^{2}J_{CP}$ = 12.3 Hz). ESI_{pos} MS *m/z* 805 $[M + 4O - H]^{+}$. Anal. calc. for $C_{44}H_{62}N_2P_4$ [742.87] C 71.14, H 8.41, N 3.77, P 16.68 %, found: C 71.09, H 8.39, N, 3.72, P, 16.55%

1,10-Di(4'-methylbenzyl)-3,8,12,17-(*RSSR*)-tetra(pyridine-2'-yl)-1,10-diaza-3,8,12,17-tetraphosphacyclooctadecane (**5**). Reaction time 24 h. Yield of **5**: 0.131 g (31 %); white solid, mp 128-130 °C. ^{1}H NMR (600 MHz, C_6D_6) δ 8.48 (ddd, $^{3}J_{HH}$ = 4.8 Hz, $^{4}J_{HH} \approx {}^{4}J_{HH} \approx$ 1.4 Hz, 4H), 7.24 – 7.29 (m, 8H), 7.01 (d, $^{3}J_{HH}$ = 7.8 Hz), 6.95 (ddd, $^{3}J_{HH}$ = 7.6 Hz, $^{4}J_{HH}$ = 2.5 Hz, $^{4}J_{HH}$ = 2.0 Hz, 4H), 6.55 (dd, $^{3}J_{HH}$ = 7.6 Hz, $^{4}J_{HH}$ = 4.8 Hz, 4H), 4.49 (d, $^{2}J_{HH}$ = 13.1 Hz, 2H), 4.00 (dm, $^{2}J_{HH}$ = 13.0 Hz, $^{2}J_{PH}$ = 2.0 Hz, 4H), 3.59 (d, $^{2}J_{HH}$ = 13.1 Hz, 2H), 3.33 (dd, $^{2}J_{HH}$ =13.0 Hz, $^{2}J_{PH}$ = 7.1 Hz, 4H), 2.18 – 2.26 (m, 4H), 2.17 (s, 6H), 2.09 – 2.14 (m, 4H), 1.90 – 2.01 (m, 8H); ^{31}P{^{1}H} NMR (242 MHz, C_6D_6) δ -31.7;

ESI_{pos} MS *m/z* 905 $[M + 4O - H]^+$. Anal. calc. for $C_{48}H_{58}N_6P_4$ [842.91] C 68.40, H 6.94, N 9.97, P 14.70 %, found: C 68.71, H 7.09, N 10.12, P 14.65 %.

1,10-Di(4'-methylbenzyl)-3,8,12,17-(*RSSR*)-tetra(pyridine-2'-yl)-3,8,12,17-tetraoxo-1,10-diaza-3,8,12,17-tetraphosphacyclooctadecane (5-O). A solution of **5** (0.050 g, 0.06 mmol) in dry toluene (5 mL) was kept under dry air for 2 weeks. The white crystalline precipitate formed was filtered off, washed with benzene and dried for 6 h at 0.01 torr. Yield of **5-O**: 0.04 g (75 %), mp 213–215 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.68 (d, $^3J_{HH}$ = 4.8 Hz, 4H), 8.07 (dd, $^3J_{HH}$ = 7.6 Hz, $^3J_{HH}$ = 4.8 Hz, 4H), 7.78 (ddm, $^3J_{HH}$ = 7.6 Hz, $^3J_{HH}$ =7.6 Hz, $^4J_{HH}$ = 1.7 Hz, $^4J_{PH}$ = 3.3 Hz, 4H), 7.34 (dd, $^3J_{HH}$ = 7.6 Hz, $^3J_{PH}$ = 8.3 Hz, 4H), 7.21 (d, $^3J_{HH}$ = 7.8 Hz, 4H), 7.08 (d, $^3J_{HH}$ = 7.8, 4H), 4.58 (d, $^2J_{HH}$ = 13.0 Hz, 2H), 4.03 (dd, $^2J_{HH}$ = 15.0 Hz, $^2J_{PH}$ = 7.5 Hz, 4H), 3.50 (d, $^2J_{HH}$ = 13.0 Hz, 2H), 2.92 (dd, $^2J_{HH}$ = 15.0 Hz, $^2J_{PH}$ = 5.5 Hz, 4H), 2.30 (s, 6H), 1.83 – 1.98 (m, 12H), 1.47 – 1.60 (m, 4H); $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$) δ 39.6; ESI_{pos} MS *m/z* 907 $[M + H]^+$; Anal. calc. for $C_{48}H_{58}N_6O_4P_4$ [906.91] C 63.57, H 6.45, N 9.27, P 13.66 %, found: C 63.51, H 6.54, N 9.20, P 13.49 %.

[(1,10-Dipropyl-3,8,12,17-(*RSSR*)-tetraphenyl-1,10-diaza-3,8,12,17-tetraphosphacyclooctadecane)nickel(II)]tetrafluoroborate (7). A solution of $[Ni(H_2O)_6](BF_4)_2$ (47.7 mg, 0.140 mmol) in dry acetonitrile (5 mL) was added to a solution of the ligand **2** (100.0 mg, 0.140 mmol) in dry acetonitrile (5 mL) and the reaction mixture was stirred overnight at ambient temperature. The volatiles were removed in vacuo, the residue was crystallized from ethyl ether, filtered off, washed with ethyl ether and dried for 5 h at 0.01 torr. Yield of **7**: 50.4 mg (38 %), 183 °C (dec.). ^{1}H NMR (400 MHz, CD_3CN) δ 7.41 (dd, $^3J_{HH}$ = 7.4 Hz, $^3J_{HH}$ = 7.4 Hz, 4H), 7.28 – 7.34 (m, 8H), 7.20 (dd, $^3J_{HH}$ = 7.7 Hz, $^3J_{HH}$ = 7.6 Hz, 8H), 3.17 (d, $^2J_{HH}$ = 13.9 Hz, 4H), 2.81 (d, $^2J_{HH}$ = 13.9 Hz, 4H), 2.51 – 2.77 (m, 16H), 2.12 – 2.14 (m, 4H), 0.93 (dq, $^3J_{HH}$ = 7.4 Hz, $^2J_{HH}$ = 13.5 Hz, 4H), 0.51 (t, $^3J_{HH}$ = 7.4 Hz, 6H); $^{31}P\{^1H\}$ NMR (162 MHz, CD_3CN) δ -6.5; $^{13}C\{^1H\}$ NMR (100 MHz, CD_3CN) δ 134.3 (br.s), 133.1 (br.s), 132.8 (s), 130.0 (s), 65.5 (dd, $^1J_{CP} \approx {}^3J_{CP} \approx$ 5.4 Hz), 56.7 (s), 26.5 (br.s), 21.4 (d, $^2J_{CP}$ = 6.9 Hz), 19.5 (s), 11.5 (s); MALDI MS *m/z* 775 $[M - 2BF_4+H]^+$. Anal. calc. for $C_{42}H_{58}B_2F_8NiN_2P_4$ [947.12] C 53.26, H 6.17, N 2.96, Ni 6.20, P 13.08%, found C 53.15, H, 6.08, N 2.75, Ni 6.32, P 13.21%.

[{1,10-Di(*tert*-butyl)-3,8,12,17-(*RSSR*)-tetraphenyl-1,10-diaza-3,8,12,17-tetraphosphacyclooctadecane}nickel(II)] tetrafluoroborate (8). 8 was prepared like complex **7**, but from ligand **4** (100.0 mg, 0.135 mmol) and $[Ni(H_2O)_6](BF_4)_2$ (45.9 mg, 0.135 mmol). Yield of **8**: 100.1 mg (76 %), mp 180 °C (dec). ^{1}H NMR (400 MHz, CD_3CN) δ 7.55 – 7.57 (m, 4H), 7.43 – 7.60 (m, 8H), 7.37 – 7.41 (m, 8H), 3.37 (d, $^2J_{HH}$ = 13.2 Hz, 4H), 3.26 (br.d, $^2J_{HH}$ = 13.2 Hz, 4H), 2.41 – 2.75 (m, 16H), 0.65 (s, 18H). ^{31}P{^{1}H} NMR (162 MHz, CD_3CN) δ -6.1; Anal. calc. for $C_{44}H_{62}B_2F_8NiN_2P_4$ [975.17] C 54.19, H 6.41, N 2.87, Ni 6.02, P 12.70 %, found C 54.23, H, 6.44, N 2.73, Ni 6.12, P 12.75%.

[{1,10-Di(4'-methylbenzyl)-3,8,12,17-(*RSSR*)-tetra(pyridine-2'-yl)-1,10-diaza-3,8,12,17-tetraphosphacyclooctadecane}nickel(II)] tetrafluoroborate (9).

9 was prepared like complex **7**, but from ligand **5** (100.0 mg, 0.119 mmol) and $[Ni(CH_3CN)_6](BF_4)_2$ (57.9 mg, 0.119 mmol). Yield of **9**: 87.8 mg (43 %). ^{1}H NMR (400 MHz, DMF-d_7) δ 8.76 (br.s, 4H, Py), 7.55 – 7.62 (m, 8H, Py), 7.34 – 7.41 (m, 4H, Py), 6.88 (d, $^3J_{HH}$ = 7.8 Hz, 4H), 6.67 (d, $^3J_{HH}$ = 7.8 Hz, 4H), 3.43 – 3.77 (m, 4H, partially overlapped by the signal of water in the solvent), 3.34 (dd, $^2J_{HH}$ = 12.4 Hz, $^2J_{PH}$ = 13.3 Hz, 4H), 3.26 (br.d, $^2J_{HH}$ = 12.4 Hz, 4H), 2.47 – 2.68 (m, 8H), 2.24 – 2.37 (m, 8H), 2.20 (s, 6H); ^{31}P{^{1}H} NMR (162 MHz, DMF-d_7) δ 11.3; ESI_{pos} MS *m/z* 903 $[M - 2\ BF_4 + H]^+$. Anal. calc. for $C_{48}H_{58}B_2F_8N_6NiP_4$ [1075.21]: C 53.62, H 5.44, N 7.82, Ni 5.46, P 11.52 %, found C 53.54, H 5.46, N 7.94, Ni 5.58, P 11.76 %.

[{1,10-Di((*R*)-(1'-phenylethyl)-3,8,12,17-(*RSSR*)-tetra(4-methylpyridine-2'-yl)-1,10-diaza-3,8,12,17-tetraphosphacyclooctadecane}nickel(II)] tetrafluoroborate (10). A solution of 1,4-bis[(hydroxymethyl)(4'-methylpyridine-2-yl)phosphino]butane (2.47 mmol) (obtained *in situ* by heating of a mixture of 1,4-bis(4'-methylpyridine-2-yl)phosphino)butane (0.75 g, 2.47 mmol) and paraformaldehyde (0.15 g, 4.9 mmol) at 100 to 110 °C on the oil bath up to homogenization) and (*R*)-(1'-phenylethyl)amine (0.30 g, 2.48 mmol) in DMF (10 mL) was stirred at 80 °C on the oil bath for 24 h. The reaction mixture was cooled and the solvent was fully evaporated in vacuo. The residue containing a mixture of isomers **6** was dissolved in dry acetonitrile and $[Ni(CH_3CN)_6](BF_4)_2$ (1.18 g, 2.46 mmol) in dry acetonitrile (5 mL) was added. The reaction mixture was stirred overnight at ambient temperature. The volatiles were removed in vacuo, the residue was crystallized from ethyl ether, filtered off, washed with

ethyl ether and dried for 5 h at 0.01 torr. Yield of **10**: 64.3 mg (23 %) . ^{1}H NMR (600 MHz, DMF-d_7) δ 8.67 (br.s, $^{3}J_{HH} \approx 4.9$ Hz, 4H), 7.42 (br.dd, $^{3}J_{HH} \approx {}^{3}J_{HH} \approx 6$ Hz, 4H), 7.19 – 7.22 (m, 6H), 7.13 – 7.16 (m, 4H), 6.99 – 7.03 (br.s, 2H), 6.93 – 6.97 (br.s, 2H), 3.59 – 3.69 (m, 2H, partially overlapped by the signal of water in the solvent), 3.30 (d, $^{2}J_{HH}$ = 13.4 Hz, 4H), 3.24 (d, $^{2}J_{HH}$ = 13.4 Hz, 4H), 2.76 – 2.83 (m, 4H, partially overlapped by the signal of the solvent), 2.39 – 2.67 (m, 12H), 0.97 (d, $^{3}J_{HH}$ = 6.8 Hz, 3H), 0.82 (d, $^{3}J_{HH}$ = 6.5 Hz, 3H); ^{31}P{^{1}H} NMR (242 MHz, DMF-d_7) δ 7.7; ESI_{pos} MS *m/z* 957 $[M - 2\ BF_4+H]^+$. Anal. calc. for $C_{52}H_{66}B_2F_8N_6NiP_4$ [1130.37]: C, 55.21; H, 5.88; N, 7.43; Ni, 5.19; P, 10.95 %, found C 55.55, H 5.87, N 7.49, Ni 5.43, P 11.06 %.

Notes

The authors declare no competing financial interest.

Supporting Information. NMR spectra and X-ray crystallography details are reported in the supporting information. X-ray crystallographic information is available through CCDC 2002519 (**1**), 2002520 (**3**), 2002521 (**4**), 2003204 (**5-O**), 2002522 (**7**), 2003205 (**9**) and 2003207 (**10**).

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References

1. Hiraoka, M. *Crown Ethers and Analogous Compounds. In Studies in organic Chemistry*. Elsevier: Amsterdam, 1992.
2. Steed, J.W.; Atwood, J.L. *Supramolecular chemistry*. John Wiley and Sons. Ltd., 2000.
3. Gloe, K. *Macrocyclic chemistry*. Springer: Dordrecht, The Netherlands, 2005.
4. Lehn, J.-M. *Supramolecular chemistry: Concepts and Perspectives.* VCH Verlagsgesellschaft mbH, 1995.
5. Caminade, A.-M. Synthesis of phosphorus-containing macrocycles and cryptands / A.-M.Caminade, J.P. Majoral. *Chem. Rev*. **1994**, *94*, 1183 – 1213

6. Pearson, R. G. Hard and Soft Acids and Bases. *J. Am. Chem. Soc.* **1963,** *85*, 3533 – 3539
7. Karasik, A.A.; O.G. Sinyashin. Phosphorus Based Macrocyclic Ligands: Synthesis and Applications. In *Catalysis by metal complexes. Vol. 37. Phosphorus Compounds: Advanced Tools in Catalysis and Material Sciences*. Gonsalvi, L.; Peruzzini, M. Eds., Springer: Dordrecht, The Netherlands, 2011, Ch.12, pp. 375 – 444.
8. Rowan, S.J.; Cantrill, S.J.; Cousins, G.R.L.; Sanders, J.K.M.; Stoddart, J.F. Dynamic Covalent Chemistry. *Angew. Chem. Int. Ed*. **2002**, *41*, 898 – 952
9. Lehn, J.-M. From supramolecular chemistry towards constitutional dynamic chemistry and adaptive chemistry. *Chem. Soc. Rev*. **2007**, *36*, 151 – 160.
10. Lehn, J.-M. Constitutional dynamic chemistry: bridge from supramolecular chemistry to adaptive chemistry. In: *Constitutional Dynamic Chemistry. Topics in Current Chemistry*, Barboiu, M. Ed., Springer: Berlin, Heidelberg, 2012, Vol. 322, pp. 1 – 32.
11. Jin, Y.; Yu, C.; Denman, R.J.; Zhang, W. Recent advances in dynamic covalent chemistry. *Chem. Soc. Rev*. **2013**, *42*, 6634 – 6654.
12. Schaufelberger, F.; Timmer, B.J.J.; Ramström, O. Principles of Dynamic Covalent Chemistry. In: D*ynamic Covalent Chemistry: Principles, Reactions, and Applications*. Zhang, W.; Jin, Y.; Eds., John Wiley & Sons, Ltd.: Chichester, 2017, Ch.1, pp. 1 – 30.
13. Jin, Y.; Wang, Q.; Taynton, Ph.; Zhang, W. Dynamic covalent chemistry approaches toward macrocycles, molecular cages, and polymers. *Acc. Chem. Res*. **2014**, *47*, 1575 - 1586
14. Cougnons, F.B.L.; Sanders, J.K.M. Evolution of Dynamic Combinatorial Chemistry. *Acc. Chem. Res*. **2012**, 45, 2211 – 2221.
15. Belowich, M.E.; Stoddart, J.F. Dynamic Imine Chemistry. *Chem. Soc. Rev.* **2012**, *41*, 2003 – 2024.
16. Li, Y.-Y.; Yu, S.-L.; Shen, W.-Y.; Gao, J.-X. Iron-, Cobalt-, and Nickel-Catalyzed Asymmetric Transfer Hydrogenation and Asymmetric Hydrogenation of Ketones. *Acc. Chem. Res*. **2015**, *48*, 2587 – 2598.

17. Yu, S. L.; Shen, W.Y.; Li, Y.Y.; Dong, Z.R.; Xu, Y.Q.; Li, Q.; Zhang, J.N.; Gao, J.X. Iron-Catalyzed Highly Enantioselective Reduction of Aromatic Ketones with Chiral P_2N_4-Type Macrocycles. *Adv. Synth. Catal*. **2012**, *354*, 818 – 822.
18. Misal Castro, L.C.; Li, H.; Sortais, J.-B.; Darcel, C. When iron met phosphines: a happy marriage for reduction catalysis. *Green Chem*. **2015**, *17*, 2283 – 2303.
19. Li, Y.; Yu, S.; Wu, X.; Xiao J.; Shen, W.; Dong, Z.; Gao, J. Iron Catalyzed Asymmetric Hydrogenation of Ketones. *J. Am. Chem. Soc*. **2014**, *136*, 4031 – 4039.
20. Saunders, A.J.; Crossley, I.R.; Colesz, M.P.; Roe, S.M. Facile self-assembly of the first diphosphametacyclophane. *Chem. Commun*. **2012**, *48*, 5766 – 5768
21. Mikhailine, A.; Lagaditis, P.O.; Sues, P.E.; Lough, A.J.; Morris, R.H. New cyclic phosphonium salts derived from the reaction of phosphine-aldehydes with acid. *J. Organomet. Chem*. **2010**, *695*, 1824 – 1830
22. Musina, E.I.; Karasik, A.A.; Sinyashin, O.G.; Nikonov, G.N. Heterocyclic Phosphines with P-C-X Fragments (X = O, N, P). In *Adv. Heterocyclic Chem*. Scriven, E.; Ramsden, Ch. Eds., Academic Press, 2015, Vol.117, pp. 83 – 130.
23. Musina, E.I.; Naumov, R.N.; Kanunnikov, K.B.; Dobrynin, A.B.; Gomez-Ruiz, S.; Lönnecke, P.; Hey-Hawkins, E.; Karasik, A.A.; Sinyashin, O.G. Chiral [16]-ane P_4N_2 macrocycles: stereoselective synthesis and unexpected intermolecular exchange of endocyclic fragments. *Dalton Trans*. **2018**, *47*, 16977 – 16984.
24. Musina, E.I.; Wittmann, T.I.; Lönnecke, P.; Hey-Hawkins, E.; Karasik, A.A.; Sinyashin, O.G. Novel representatives of 16-membered aminomethylphosphines with alkyl substituents at nitrogen and their gold(I) complexes. *Russ. Chem. Bull*. **2018**, *67*, 328 – 335.
25. Musina, E.I.; Wittmann, T.I.; Latypov, Sh.K.; Kondrashova, S.A.; Lönnecke, P.; Litvinov, I.A.; Hey-Hawkins, E.; Karasik, A.A. Self-assembly of chiral 1,8-diaza-3,6,10,13-tetraphosphacyclotetradecanes via dynamic transformation of 7- and 14-membered aminomethylphosphines. *Eur. J. Inorg. Chem*. **2019**, *2019*, 3053 – 3060
26. Musina, E. I.; Fesenko, T. I.; Strelnik, I. D.; Polyancev, F. M.; Latypov, Sh. K.; Lönnecke, P.; Hey-Hawkins, E.; Karasik, A. A.; Sinyashin, O. G. Synthesis and

unique reversible splitting of 14-membered cyclic aminomethylphosphines on to 7-membered heterocycles. *Dalton Trans*. **2015**, *44*, 13565 – 13572.

27. Naumov, R.N.; Musina, E.I.; Kanunnikov, K.B.; Fesenko, T.I.; Krivolapov, D.B.; Litvinov, I.A.; Lönnecke, P.; Hey-Hawkins, E.; Karasik, A.A.; Sinyashin, O.G. Alternating stereoselective self-assembly of *SSSS*/*RRRR* or *RSSR* isomers of tetrakisphosphines in the row of 14-, 16-, 18- and 20-membered macrocycles *Dalton Trans*. **2014**, *43*, 12784 – 12789.
28. Wittmann, T.I.; Musina, E.I.; Krivolapov, D.B.; Litvinov, I.A.; Kondrashova, S.A.; Latypov, Sh.K.; Karasik, A.A.; Sinyashin, O.G. Covalent self-assembly of the specific *RSSR* isomer of 14-membered tetrakisphosphine. *Dalton Trans*. **2017**, *46*, 12417 – 12420.
29. Musin, L.I.; Musina, E.I.; Kryvolapov, D.B.; Karasik, A.A.; Sinyashin, O.G. New 18-membered tetrakisphosphine macrocycle and its derivatives. *Phosphorus, Sulfur Silicon Relat. Elem*. **2016**, *191*, 1591 – 1592
30. Corbridge, D.E.C. *Phosphorus: Chemistry, Biochemistry and Technology, Sixth Edition*. Taylor & Francis Group, 2013.
31. Musina, E.I.; Wittmann, T.I.; Dobrynin, A.B.; Lönnecke, P.; Hey-Hawkins, E. Karasik, A.A.; Sinyashin, O.G. Macrocyclic tetrakis-phosphines and their copper(I) complexes. *Pure Appl. Chem*. **2017**, *89*, 331 – 339.
32. Marsh, R.E. Space group *P*1: an update. *Acta Crystallogr., Sect. B: Struct. Sci., Cryst. Eng. Mater.* **2005**, *61*, 359.
33. Mealli, C.; Sabat, M.; Zanobini, F.; Ciampolini, M.; Nardi, N. Macrocyclic polyphosphane ligands. Iron(II), cobalt(II), and nickel(II) complexes of (4*RS*,7*RS*,13*SR*,16*SR*)-tetraphenyl-1,10-dipropyl-1,10-diaza-4,7,13,16-tetraphosphacyclooctadecane: crystal structures of their tetraphenylborate derivatives. *J. Chem. Soc., Dalton Trans*. **1985**, 479 – 485
34. Musina, E.I.; Shamsieva, A.V.; Strelnik, I.D.; Gerasimova, T.P.; Krivolapov, D.B.; Kolesnikov, I.E.; Grachova, E.V.; Tunik, S.P.; Bannwarth, C.; Grimme, S.; Katsyuba S.A.; Karasik, A.A.; Sinyashin, O.G. Synthesis of novel pyridyl containing phospholanes and their polynuclear luminescent copper(I) complexes. *Dalton Trans.* **2016**, *45*, 2250 – 2260.

35. Dickson, R.S.; Elmes, P.S.; Jackson, W.R. Further Improvements in the Preparation of Disecondary Phosphines $PhHP(CH_2)_nPHPh$, n = 2, 3, and Their Tetracarbonyltungsten Complexes: Analysis of Their Multinuclear NMR Spectra. O*rganometallics.* **1999**, *18,* 2912 – 2914

Table of Contents graphic