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Covalent self-assembly of the specific *RSSR* isomer of 14-membered tetrakisphosphine†

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The first representative of the specific *RSSR* isomer of 14-membered tetrakisphosphine has been obtained instead of the *RRRR/SSSS* isomer predicted according to the empirical rule formulated recently. The geometry of the obtained 14-P_4N_2 is preorganized for the dicopper complex formation with the unique coordination mode in the row of P_4N_2 corands.

Macrocyclic polyphosphines exist as a rule as mixtures of diastereomers due to the high inversion barrier of phosphorus atoms in phosphines (150 kJ mol^{-1}). The separation of these mixtures and isolation of individual isomers in a pure state is a serious obstacle for the use of macrocyclic phosphines in coordination and supramolecular chemistry, as well as in catalysis.[1] We have proposed the stereoselective synthesis of macrocyclic tetrakisphosphines *via* the covalent self-assembly approach by the condensation of 1,*n*-bisphosphinealkanes (*n* = 2–5) with formaldehyde and primary amines. This method of the design of macrocyclic polyphosphines was successfully used for the stereoselective synthesis of more than forty representatives of 14-, 16-, 18- and 20-membered macrocyclic P_4N_2 corands.[2] According to the Le Bel–van't Hoff rule, the maximum number of isomers for four asymmetric atoms is 2^4, whereas the number of diastereoisomers for tetrakisphosphines is five. Nevertheless instead of five possible diastereomers only one stereoisomer of 14-, 16-, 18- and 20-P_4N_2 was isolated from reaction mixtures in good or moderate yield. The crystal structure analysis of the at least thirty isolated P_4N_2 corands allowed us to formulate the empirical rule which predicted the configuration of the phosphorus atoms in the macrocyclic tetrakisphosphine corands.[3] So, if the two chiral phosphorus centers in the macrocycle are linked by an odd

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number of methylene groups, then the $R_PS_PS_PR_P$ stereoisomer is adopted, that is realized for 16- and 20-membered corands. If the phosphorus atoms in the macrocycle are linked by an aliphatic chain consisting of an even number of methylene groups, then the racemic $S_PS_PS_PS_P/R_PR_PR_PR_P$ isomer is formed.[3]

The selectivity of the proposed synthetic approach may be explained by covalent self-assembly phenomena. The distinctive feature of the covalent self-assembly processes is their ability of self-correction when the "incorrect" intermediate is able to decompose into starting compounds due to the reversibility of the reaction. These compounds react further to give a more thermodynamically stable "correct" product. The reaction mixtures of secondary bisphosphines with formaldehyde and primary amines contain many products but only one of them is crystallized at the final stage.

It should be mentioned that in contrast to the 16-, 18 and 20-membered macrocycles, which are formed from 1,*n*-(bisphosphine)propane, butane and pentane[4] either 1-aza-3,6-diphosphacycloheptanes[5] or 14-membered tetrakisphosphines[6] are formed in the course of interaction of 1,2-bis(phenylphosphino)ethane, formaldehyde and primary alkyl- and alkylarylamine. It was shown that dissolving of 14-P_4N_2 macrocycles led to the splitting of the macrocycle into the *RS*- and *RR/SS* isomers of 1-aza-3,6-diphosphacycloheptane.[6] The higher homologues of P_4N_2-macrocycles are only stereoisomerized in solutions to some extent.[4] The lability of P–CH$_2$–N fragments in cyclic and macrocyclic aminomethylphosphines is responsible for the reversibility of the condensation reaction whereas crystallization is a driving force of the stereoselective formation of aminomethylphosphine macrocycles.

Despite the presence of different isomers of P_4N_2 corands in the reaction mixtures all attempts to isolate the isomers which are the exception to the empirical rule were unsuccessful. Here we represent the first example of the unexpected *RSSR* isomer of 14-membered macrocyclic aminomethylphosphine and its dicopper complex. The interaction of 1,2-bis(phenylphosphino)ethane (**1**) with formaldehyde and iso-
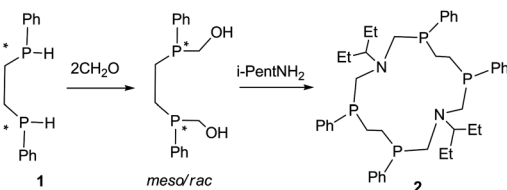
Scheme 1 Synthesis of macrocycle **2**.

pentylamine in DMF (Scheme 1) as expected led to the mixture of products. The ^{31}P NMR spectrum of the reaction mixture showed that several products are formed but three signals have prevailed. According to 2D ^{31}P DOSY spectra (Fig. S9 and S10, ESI†) the signals at −23.9 ppm and −27.0 ppm have a higher self-diffusion coefficient than the signal at −34.4 ppm, therefore, the first two signals belong to the *rac*- and *meso*-isomers of seven-membered cycles as the products of "1 + 1" cyclocondensation, while the signal at −34.4 ppm corresponds to the 14-membered macrocycle as a "2 + 2" cyclocondensation product. A variety of NMR correlation experiments (^{1}H–^{1}H COSY, ^{1}H–^{13}C HSQC, ^{1}H–^{13}C/^{31}P HMBC, 2D ^{31}P and ^{1}H DOSY, 1D NOESY)[9–12] let us prove this hypothesis (Fig. S1–S10, ESI†).

The macrocycle **2** was isolated as white crystals after complete removal of DMF from the reaction mixture and the crystallization of the residue from ether in 21% yield. The ESI mass-spectrometry data of compound **2** (m/z 778 [M + 4O]$^{+}$) confirm the macrocycle formation. The comparative analysis of the ^{31}P and ^{1}H NMR spectra of the macrocycle **2** and the earlier obtained *RRRR/SSSS*-isomers of 1,8-diaza-3,6,10,13-tetra-phosphacyclotetradecanes[6] allows us to suppose their different structures. Namely, in the ^{31}P NMR spectrum the pure macrocycle **2** (C_6D_6, 303 K) resonates at the higher field (δ_P −34.4 ppm) than the previously described *RRRR/SSSS*-isomers of 14-P_4N_2 corands (δ_P −31.0 to −31.9 ppm). But the most spectacular is the transformation of the P–CH$_2$–CH$_2$–P methylene proton resonances (AA′BB′ system) in the ^{1}H{^{31}P} NMR spectra (Fig. 1). In the case of the *RRRR/SSSS* isomer these protons resonate *ca.* as doublet of doublets in ^{1}H{^{31}P} spectra due to two

relatively large vicinal spin–spin couplings (SSC) (*e.g.* for 14-P^{Ph_4}N$^{i-Pr_2}$, Fig. 1a), however in the macrocycle **2** these protons are observed as two multiplets due to the essentially smaller vicinal SSC (Fig. 1b).

This is a clear indication that geometry of the P–CH$_2$–CH$_2$–P moieties in these compounds is different.

Namely, while in the 14-P^{Ph_4}N$^{i-Pr_2}$ these fragments have *trans* conformation (Fig. 1c) and therefore there are two relatively large J_{HH} (geminal and vicinal) for each proton. In the compound **2** these fragments, presumably, have conformation with two *gauche* orientations of phosphorus (Fig. 1d), and as a result, SSCs between vicinal protons should be averaged and small. Moreover, a lack of strong NOE's (Fig. S7, ESI†) between N–CHEt$_2$ and P–CH$_2$–CH$_2$–P protons indicates that *N*-isopentyl substituents are directed out of the macrocycle cavity unlike the *N*-isopropyl substituents in the *RRRR/SSSS*-isomer of 14-P^{Ph_4}N$^{i-Pr_2}$. Thus one can conclude that the structure of the compound **2** is different from the structure of the *RRRR/SSSS*-isomer, and it is the *RSSR/SRRS*-isomer.

This hypothesis is in full agreement with the results of X-ray analysis of the crystal **2** (Fig. 2). The crystallographic data and the selected bond lengths and angles for **2** are given in Tables S1 and S2 (ESI).†

Macrocycle **2** is an *RSSR*-stereoisomer and it has an unfolded conformation (Fig. 2). The P1⋯P2 and P1⋯P2′ distances (3.466(3) Å and 4.162(3) Å respectively) are significantly less than that for the *RRRR/SSSS* isomer (4.4774(3) Å and 4.7381(4) Å respectively),[6] whereas the N1⋯N1′ distance (7.125(6) Å) is significantly more than that for the *RRRR/SSSS* isomer (5.103(1) Å).[6] Four phosphorus atoms form the macrocyclic plane P$_4$. The nitrogen atoms slightly deviate from the P$_4$ plane (the deviation is 0.209 Å) and they are located up and down relative to it. Unlike the *RRRR/SSSS* isomer, the exocyclic substituents in the *RSSR*-isomer **2** are in an equatorial position relative to the macrocyclic plane, and the *ipso*-C-atoms of phenyl substituents lie in the P$_4$ plane. The lone electron pairs (LPs) of the two neighboring phosphorus atoms P1′ and P$_2$ or P$_1$ and P$_2$′ are in the axial position and they are directed on one side of the macrocycle plane. As a result of the centrosymmetric conformation of the molecule **2**, the LPs of two
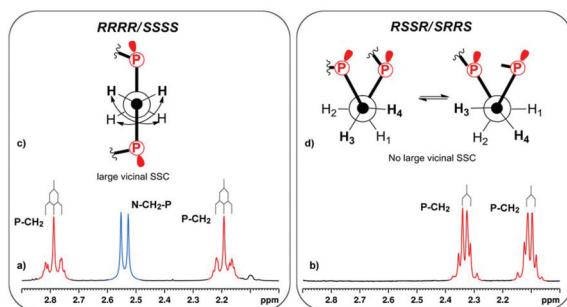

Fig. 1 Fragment of ^{1}H {^{31}P} NMR spectra of 14-P^{Ph_4}N$^{i-Pr_2}$ (a) and 14-P^{Ph_4}N$^{i-Pent_2}$ (**2**) (b) in C_6D_6 at T = 303 K. Newman projections of the P–CH$_2$–CH$_2$–P protons of 14-P^{Ph_4}N$^{i-Pr_2}$ (c) and 14-P^{Ph_4}N$^{i-Pent_2}$ (**2**) (d) macrocycles, respectively.
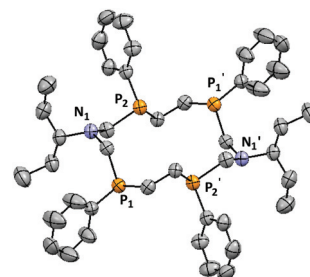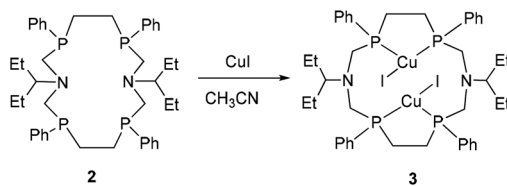

Fig. 2 Molecular structure of *RSSR*-isomer of compound **2** (hydrogen atoms are omitted for clarity). ORTEP drawing, thermal ellipsoids with 50% probability level. Molecule in the special position on the center of symmetry (1 − x, 1 − y, 1 − z).

Scheme 2 Synthesis of complex **3**.

Fig. 3 Molecular structure of complex **3** (hydrogen atoms are omitted for clarity). ORTEP drawing, thermal ellipsoids with 50% probability level. Molecule in the special position on the center of symmetry ($1 - x$, $1 - y$, $1 - z$).

other phosphorus atoms P_1 and P_2' have the opposite direction. So, unlike the "*anti–anti–anti*" position of LPs in the *RRRR/SSSS* isomer the "*syn–anti–syn*" direction of LPs of four phosphorus atoms is realized in the *RSSR*-isomer.

The *RSSR*-stereoisomer **2** is the exception to the earlier formulated empirical rule concerning the isolation of the *RRRR/SSSS* isomer only in the case of 14-P_4N_2 corands.

The geometry of the corand **2** is pre-organized for the binuclear bis-chelate complex formation. Recently we demonstrated that the initial conformation of the P_4N_2 corands and arrangement of the phosphorus LPs define the structure of formed metal complexes.[8] In particular, the *RRRR/SSSS* isomer of the 14-membered macrocycle with an "*anti–anti–anti*" position of the phosphorus LPs reacts with copper(I) salts as a P_4 tetradentate ligand giving the mononuclear copper complexes independent of the metal : ligand ratio.[7,8]

The interaction of *RSSR* isomer **2** with CuI in CH_3CN results in the complex **3** in a good yield of 52% (Scheme 2). It should be mentioned that the complex **3** is formed as a major product independent of the metal to ligand ratio in the reaction mixture. The ESI mass-spectrometry data and elemental analysis of **3** are in good agreement with the proposed Cu_2I_2L composition of complex **3**.

The singlet (-31.8 ppm) in the ^{31}P {^1H} and quite simple $^1H/^{13}C$ spectra (one set of signals for each fragment) suggests a high overall symmetry of the complex. The variety of homo- and heteronuclear NMR correlation experiments (Fig. S11–S15, ESI†) allows establishing the structure almost directly. It is important that the multiplet pattern of the endocyclic P–CH_2–CH_2–P protons in the ^1H {^{31}P} NMR spectrum of **3** is similar to that of the free ligand **2** and it indicates the retaining of the macrocyclic ring structure and the phosphorus atom configuration (Fig. S11, ESI†). Moreover, illegible NOE's between the N–R and the endocyclic protons (Fig. S16–S18, ESI†) suggest the out-orientation of these groups relative to the macrocycle cavity.

The structure of **3** was determined by single crystal X-ray diffraction (Fig. 3). The crystallographic data and the selected bond lengths and angles for **3** are given in Tables S1 and S2 (ESI).† Compound **3** is a neutral dicopper bis-P,P-chelate complex. In contrast to the previously reported complexes of 16-, 18- and 20-P_4N_2 corands[8] in complex **3** each copper atom is coordinated by two phosphorus atoms of P–CH_2–CH_2–P fragments to form a very stable five-membered chelate cycle whereas in complexes with 16-, 18- and 20-P_4N_2 corands each copper atom is bonded by two phosphorus atoms of P–CH_2–
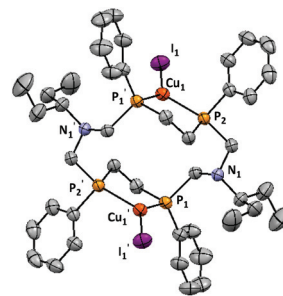
N–CH_2–P fragments and a six-membered chelate is formed. It is a principal difference between these complexes because the P_4N_2 ligand is forced to change its own structure and the configuration of the phosphorus atoms in the case of 16-, 18- and 20-membered complexes, whereas in complex **3** the ligand retains the stereoisomeric form of the free ligand.

The five-membered chelate metallocycles in complex **3** have a twist-conformation. Copper atoms have a trigonal planar configuration (the sum of the bond angles is 358.33(2)°). Both the Cu–I fragments are perpendicular to the P_4 plane and they are directed opposite to each other. The bond lengths P_1–Cu_1 and P_2–Cu_2 are 2.2524(7) Å and 2.2783(7) Å respectively, similar to the P–Cu bond lengths in dicopper complexes of 16-, 18- and 20-membered macrocycles.[8] The values of the Cu_1–I_1 length (2.4591(5) Å), angle P_1–Cu_1–P_2 (91.04(2)°) and the distance $P_1 \cdots P_2$ (3.233(1) Å) in the five-membered chelate metallocycle of **3** are less than the parameters for the six-membered chelates in the dicopper complexes of 16-, 18- and 20-P_4N_2 macrocycles.

In summary, the first example of the unexpected *RSSR* isomer of 1,8-diaza-3,6,10,13-tetraphosphacyclotetradecanes has been obtained by the condensation reaction of 1,2-bis(phenylphosphino)ethane, formaldehyde and iso-pentylamine as a covalent self-assembly product. Obviously the crystallization plays an important role in the isolation of the unexpected *RSSR*-isomer. We demonstrated that the arrangement of phosphorus lone electron pairs in the *RSSR* isomer of the 14-P_4N_2 ligand defines its bis-P,P-chelate coordination mode in the CuI complex without ligand conformation changes.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

Notes and references

1 (a) A.-M. Caminade and J. P. Majoral, *Chem. Rev.*, 1994, **94**, 1183; (b) M. Pabel and B. Wild, *Comp Hetecycl Chem II*, 1996, p. 947; (c) A.-M. Caminade and J. P. Majoral, *Synlett*, 1996, 1019; (d) I. Bauer, W. D. Habicher, I. S. Antipin and O. G. Sinyashin, *Russ. Chem. Bull.*, 2004, **53**, 1402; (e) V. Simulescu and G. Ilia, *J. Inclusion Phenom. Macrocyclic Chem.*, 2010, **66**, 3; (f) A. A. Karasik and O. G. Sinyashin, in *Phosphorus Compounds Advanced Tools in Catalysis and Material Sciences*, ed. M. Peruzzini and L. Gonsalvi, Springer, Netherlands, 2011, vol. 37(12), p. 375; (g) C. D. Swor and D. R. Tyler, *Coord. Chem. Rev.*, 2011, **255**, 2860; (h) E. I. Musina, A. A. Karasik, O. G. Sinyashin and G. N. Nikonov, *Advances in Heterocyclic Chemistry*, Academic Press, 2015, p. 83.

2 (a) A. A. Karasik, A. S. Balueva and O. G. Sinyashin, *C. R. Chimie*, 2010, **13**, 1151; (b) D. V. Kulikov, A. A. Karasik, A. S. Balueva, O. N. Kataeva, I. A. Livinov, E. Hey-Hawkins and O. G. Sinyashin, *Mendeleev Commun.*, 2007, **17**, 195; (c) A. S. Balueva, D. V. Kulikov, R. M. Kuznetsov, A. T. Gubaidullin, L. Ricard, A. A. Karasik and O. G. Sinyashin, *J. Inclusion Phenom. Macrocyclic Chem.*, 2008, **60**, 321; (d) R. N. Naumov, A. A. Karasik, K. B. Kanunnikov, A. V. Kozlov, Sh. K. Latypov, K. V. Domasevitch, E. Hey-Hawkins and O. G. Sinyashin, *Mendeleev Commun.*, 2008, **18**, 80; (e) R. N. Naumov, A. A. Karasik, O. G. Sinyashin, P. Lönnecke and E. Hey-Hawkins, *Dalton Trans.*, 2004, 357; (f) A. A. Karasik, D. V. Kulikov, A. S. Balueva, S. N. Ignat'eva, O. N. Kataeva, P. Lönnecke, A. V. Kozlov, Sh. K. Latypov, E. Hey-Hawkins and O. G. Sinyashin, *Dalton Trans.*, 2009, 490; (g) R. N. Naumov, A. V. Kozlov, K. B. Kanunnikov, S. Gomez-Ruiz, E. Hey-Hawkins, Sh. K. Latypov, A. A. Karasik and O. G. Sinyashin, *Tetrahedron Lett.*, 2010, **51**, 1034; (h) A. A. Karasik, D. V. Kulikov, R. M. Kuznetsov, A. S. Balueva, S. N. Ignat'eva, O. N. Kataeva, P. Lönnecke, O. G. Sharapov, Sh. K. Latypov, E. Hey-Hawkins and O. G. Sinyashin, *Macroheterocycles*, 2011, **4**, 324; (i) C. D. Swor and D. R. Tyler, *Coord. Chem. Rev.*, 2011, **255**, 2860.

3 R. N. Naumov, E. I. Musina, K. B. Kanunnikov, T. I. Fesenko, D. B. Krivolapov, I. A. Litvinov, P. Lönnecke, E. Hey-Hawkins, A. A. Karasik and O. G. Sinyashin, *Dalton Trans.*, 2014, **43**, 12784.

4 A. A. Karasik, R. N. Naumov, K. B. Kanunnikov, D. B. Krivolapov, I. A. Litvinov, P. Lönnecke, A. S. Balueva, E. I. Musina, E. Hey-Hawkins and O. G. Sinyashin, *Macroheterocycles*, 2014, **7**, 181.

5 E. I. Musina, A. A. Karasik, A. S. Balueva, I. D. Strelnik, T. I. Fesenko, A. B. Dobrynin, T. P. Gerasimova, S. A. Katsyuba, O. N. Kataeva, P. Lönnecke, E. Hey-Hawkins and O. G. Sinyashin, *Eur. J. Inorg. Chem.*, 2012, **11**, 1857.

6 E. I. Musina, T. I. Fesenko, I. D. Strelnik, F. M. Polyancev, S. K. Latypov, P. Lönnecke, E. Hey-Hawkins, A. A. Karasik and O. G. Sinyashin, *Dalton Trans.*, 2015, **44**, 13565.

7 T. I. Fesenko, E. I. Musina, A. A. Karasik and O. G. Sinyashin, *Phosphorus, Sulfur Silicon Relat. Elem.*, 2015, **190**, 824.

8 E. I. Musina, T. I. Wittmann, P. Lönnecke, E. Hey-Hawkins, A. A. Karasik and O. G. Sinyashin, *Pure Appl. Chem.*, 2017, **89**, 331.

9 E. Derome, *Modern NMR Techniques for Chemistry Research*, Pergamon, Cambridge, U.K., 1988.

10 Atta-ur-Rahman, *One and Two Dimensional NMR Spectroscopy*, Elsevier, Amsterdam, 1989.

11 K. Stott, J. Stonehouse, J. Keeler, T. L. Hwang and A. J. Shaka, *J. Am. Chem. Soc.*, 1995, **117**, 4199–4200.

12 D. H. Wu, A. D. Chen and C. S. Johnson, *J. Magn. Reson., Ser. A*, 1995, **115**, 260–264.