Self-assembling squares with amino acid-decorated bipyridines: heterochiral self-sorting of dynamically interconverting diastereomers†‡

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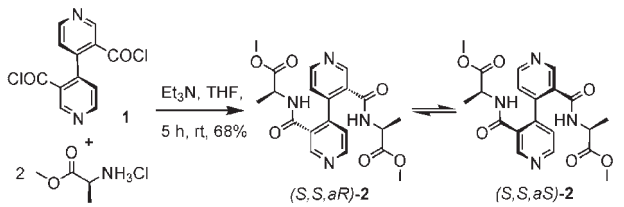
Heterochiral self-sorting into only one stereoisomer is observed when metallo-supramolecular squares self-assemble from amino acid-substituted, dynamically interconverting bipyridine stereoisomers and dpppM(OTf)$_2$ corners (M = Pd, Pt).

Particularly interesting among self-assembled[1] metallo-supramolecular complexes[2] are chiral ones[3] such as those reported earlier by Stang,[4] Lin,[5] and ourselves.[6] Self-assembly processes are hard to predict when racemates of building blocks[2] are used. Both, homochiral assembly formation from racemic building blocks (self-recognition)[7] and heterochiral assembly formation (self-discrimination)[8] are quite rare. Quickly interconverting diastereomers complicate this situation even more.[9] Here, we present the heterochiral self-assembly of metallo-supramolecular squares[10] from four (*S*)-alanine-decorated bipyridines **2** and four dpppM(OTf)$_2$ corners (M = Pd, Pt; Scheme 1). While the chirality of the (*S*)-alanine moieties is fixed, the chiral axis is not and the (*S*,*S*,*aS*)- and (*S*,*S*,*aR*)-bipyridine diastereomers interconvert.

3,3′-Substitution of 4,4′-bipyridine generates axially chiral enantiomers which quite easily interconvert, if the substituent size permits.[12] Diastereomers are created upon incorporation of additional chiral centers in the substituents, *e.g.* the (*S*)-alanine esters in **2**. Variable-temperature NMR experiments (supporting information) show the diastereomers of **2** to coexist in solution in ratios of 3 : 1 ($CDCl_3$) or 3 : 2 ([D_6]-acetone) and to interconvert.[13] Due to packing effects, only one diastereomer is however found in the solid-state structure.



Scheme 1 Synthesis of **2** from **1**[11] and alanine ester.

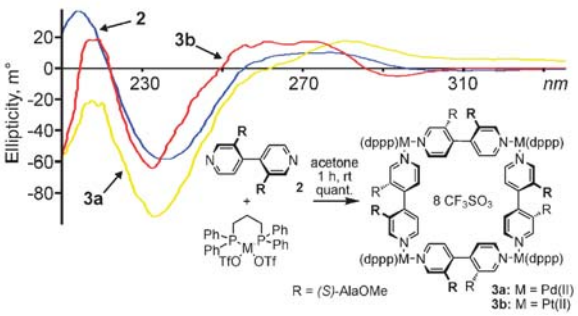


Fig. 1 Self-assembly of squares **3a,b** and CD spectra of **2** and **3a,b** (all: methanol, 5×10^{-4} M of **2**).

Except for a small, coordination-indicating shift of the 215 nm band, the CD spectra for chiral assemblies **3a,b** (Fig. 1) resemble that of **2**. In the ESI mass spectra of **3a,b** doubly and triply charged metallo-supramolecular squares are observed together with the typical[14] fragments. The mass spectra rule out other assemblies than squares.

Due to (a) the stereoisomerization of each of the four ligands and (b) the torsional angle of the biaryl bond which causes the 3,3′-substituents to either point towards or away from the square's cavity, many different isomeric structures (some conformers, some stereoisomers) can in principle coexist and interconvert in solution. As reported previously,[6] even conformers interconvert slowly on the NMR time scale due to steric hindrance of bipyridine rotation through the dppp phenyl rings. Consequently, one may expect to obtain rather complex NMR spectra for the squares under study here.

Surprisingly, this is not the case (Fig. 2). In the rather simple ^{1}H NMR spectra of **3a,b** in [D_6]-acetone, the symmetry of the ligand component within the supramolecular aggregates is reduced as compared to the free ligand **2** (two sets of signals in 1 : 1 ratio; see supporting information for spectra of **3b**). Two doublets in the ^{31}P NMR spectra of **3a,b** (1 : 1 ratio; $^2J_{PP}$ = 30.5 Hz (**3a**) and 29.8 Hz (**3b**)) confirm symmetry reduction. The coupling indicates that both P atoms at each corner differ from each other. From this finding, the symmetry of the resulting assemblies can be obtained, since only three scenarios would be in accordance with these observations: The first one would be the formation of an almost exact 1 : 1 : 1 : 1 mixture of four different, D_4-symmetric isomers coincidentally correctly mimicking the roof effect in the ^{31}P NMR spectra. This is quite unlikely compared to the other

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† Dedicated to Prof Karl-Heinz Dötz on the occasion of his 65th birthday.

‡ Electronic supplementary information (ESI) available: Synthesis and analytical data, ^{1}H-VT-NMR spectra of **2**, ^{1}H, ^{31}P NMR, HH-COSY, and HMQC spectra of **3b**, and crystal structure data. CCDC reference numbers 684938 ((*S*,*S*)-**2**), 684939 ((*R*,*R*)-**2**) and 684940 (**3b**). For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/b806916f

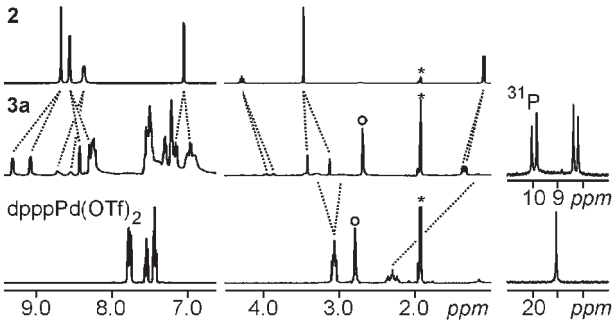

Fig. 2 Room-temperature ^{1}H (left) and ^{31}P NMR spectra (right) of **2**, **3a**, and dpppPd(OTf)$_2$ in [D$_6$]-acetone (*); circles: residual water.

alternatives which would be D_2 or C_4 symmetrical isomers that also agree with the obtained NMR results. Thus, the NMR results indicate that only one isomer is formed exclusively.

Eight from all possible candidate structures meet the criteria of the NMR experiments and can be identified from symmetry considerations (Fig. 3). Two C_4 symmetrical isomers with one amide group pointing inwards and one outwards on each ligand have a (*S*,*S*,*aR*) absolute configuration of all ligands in **I** and (*S*,*S*,*aS*) in **II**. In the six D_2-symmetric isomers, the situation is a bit more complex. In isomers **III** (all amides out) and **IV** (all amides in), two ligands are (*S*,*S*,*aR*)-configured, the other two (*S*,*S*,*aS*). In the remaining four isomers, the amide groups of two opposite ligands are pointing inside and the other two outwards: **V** (*aR* in, *aS* out), **VI** (*aS* in, *aR* out), **VII** (all *aR*) and **VIII** (all *aS*). The symmetry considerations depicted in Fig. 3 lead to the following conclusion: For C_4-symmetrical structures **I** and **II**, *each* ligand contributes to both sets of signals, since their two pyridine rings are not equivalent. For all D_2-symmetric structures, both pyridine rings in each ligand are equivalent, but the structure contains two pairs of ligands, each one of which causes one set of signals in the NMR.

2D-NMR experiments (HH-COSY, HMQC, HMBC) of **3a,b** were performed to assign all ^{1}H and ^{13}C nuclei of the ligands (supporting information) and to narrow down the number of possible isomers. In the HMBC spectrum (Fig. 4) each signal is assigned to one set (A or B). Only A/A and B/B cross signals are found. Cross signals between "A-protons"

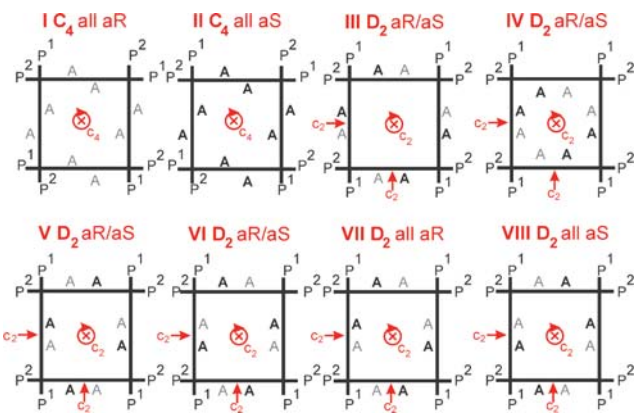

Fig. 3 Eight candidate structures that meet the NMR-derived symmetry criteria (black A: amides above; grey A: amides below square plane).

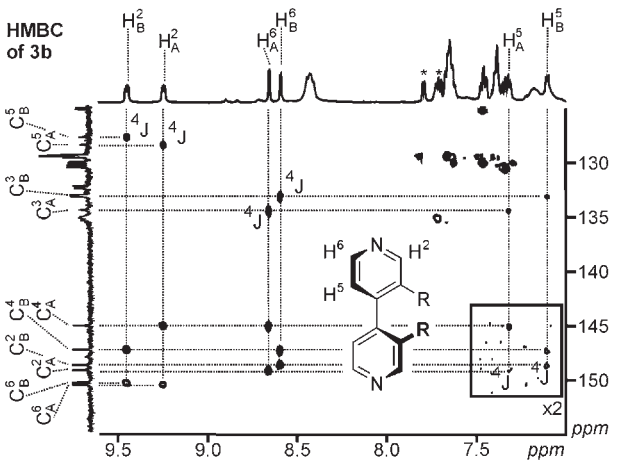

Fig. 4 The room-temperature HMBC spectrum (aromatic region) of **3b** in [D$_6$]-acetone shows cross peaks resulting from ^{3}J and ^{4}J ^{1}H-^{13}C couplings. Only the cross peaks for ^{4}J couplings are labeled.

and "B-carbons" or *vice versa* are not observed. In particular, cross signals exist for the ^{3}J couplings between H_B^5 and C_B^4 as well as H_A^5 and C_A^4. These can only appear in D_2-symmetrical isomers **III** to **VIII**, because both pyridine rings of each ligand belong to the same set of signals. In C_4-symmetrical structures **I** and **II**, H_B^5 should couple with C_A^4 and H_A^5 with C_B^4. Thus isomers **I** and **II** can be ruled out.

A discrimination between the remaining candidates is not possible by NMR experiments alone. Therefore, single crystals of **3b** were grown from saturated acetone solutions at 50 °C over three days. The crystal structure of **3b** shown in Fig. 5 clearly demonstrates the assembly to be a square with all amides pointing away from the cavity. The absolute configuration of two opposite ligands is (*S*,*S*,*aR*), while the two remaining ligands are (*S*,*S*,*aS*)-configured.§

More profound insight into this remarkable heterochiral selection comes from the solid-state structure: Crystal

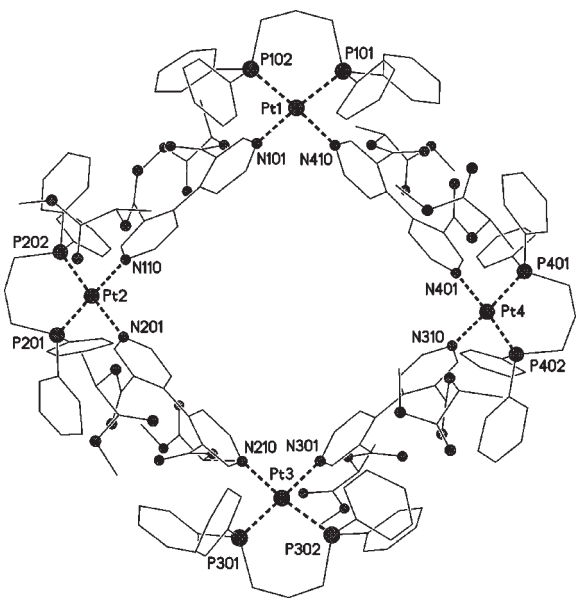

Fig. 5 Solid state structure of the cation of **3b** (hydrogen atoms omitted for clarity).

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structures of achiral squares,[8c,10b] show two of the four phenyl rings of each dppp to be π-stacked each with one pyridine ring. As visible in Fig. 5, the amino-acid substituents avoid steric congestion with the non-stacked phenyl groups in the axial positions of the diphosphametallacyclohexane rings. The dppp ligands thus dictate an [up–down]$_4$ arrangement of the amino-acid substituents. At the same time, they all point away from the cavity—likely to maximize stacking with the equatorial phenyl groups. Both arguments together unambiguously lead to the structure found in the crystal.

In conclusion, we present the remarkably diastereoselective self-assembly of metallo-supramolecular squares incorporating four bipyridine ligands each carrying two alanine substituents. NMR experiments and crystal structure agree on the formation of only one diastereomer with outwards oriented side chains and pairwise opposite bipyridines having the same axial chirality. Although the chiral centers of the alanines favor one of the axially chiral biaryl configurations in the free ligand, the ratio of both diastereomers is strictly 1 : 1 in the squares. The diastereoselectivity is not governed by the alanyl moieties any more, but largely influenced by the stereoelectronic effects of the dppp ligand which finally lead to the exclusive formation of heterochiral assemblies. The energetic preference for one of the ligand diastereomers is overridden by self-assembly-induced heterochiral self-sorting.[16]

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Notes and references

§ **Crystal structure studies**: The single-crystal X-ray diffraction studies were carried out on a Bruker-Nonius Kappa-CCD diffractometer at 123(2) K using MoK$_\alpha$ radiation (λ = 0.71073 Å). Direct methods (SHELXS-97) were used for structure solution, and full-matrix least-squares refinement on F^2 (SHELXL-97).[15] CCDC numbers 684938 ((***S*,*S*)-2**), 684939 ((***R*,*R*)-2**) and 684940 (**3b**).‡

Crystal data for (*S*,*S*)-2: $C_{20}H_{22}N_4O_6$, M = 414.42, space group $P2_12_12_1$ (No. 19), orthorhombic, a = 8.709(1), b = 11.104(1), c = 21.032(3) Å, V = 2033.9(4) Å^3; Z = 4; $\rho_{ber.}$ = 1.353 g cm^{-3}; μ (MoK$_\alpha$) = 0.102 mm^{-1}, F(000) = 872, 33 705 reflections ($2\theta_{max}$ = 55°) measured (4640 unique, R_{int} = 0.045), R(for $I > 2\sigma(I)$) = 0.0298, w$R2$(all data) = 0.0752, GOF = 1.053 for 279 parameters and 2 restraints, largest diff. peak and hole 0.261 e Å^{-3}/−0.185 eÅ^{-3}.

Crystal data for (*R*,*R*)-2: $C_{20}H_{22}N_4O_6$, M = 414.42, space group $P2_12_12_1$ (No. 19), orthorhombic, a = 8.732(1), b = 11.123(1), c = 21.076(2) Å, V = 2047.0(4) Å^3; Z = 4; $\rho_{ber.}$ = 1.345 g cm^{-3}; μ (MoK$_\alpha$) = 0.101 mm^{-1}, F(000) = 872, 29 007 reflections ($2\theta_{max}$ = 55°) measured (4671 unique, R_{int} = 0.067), R(for $I > 2\sigma(I)$) = 0.0414, w$R2$(all data) = 0.0991, GOF = 1.088 for 279 parameters and 2 restraints, largest diff. peak and hole 0.254 e Å^{-3}/−0.243 e Å^{-3}.

Crystal data for 3b: $[C_{188}H_{192}N_{16}O_{24}P_8Pt_4]^{8+}\cdot 8[CF_3SO_3]^-\cdot 7C_3H_6O$, M = 5686.80, space group $P2_1$ (No. 4), monoclinic, a = 14.955(1), b = 27.472(1), c = 31.536(3) Å, β = 100.57(1)°, V = 12 737(2) Å^3; Z = 2; $\rho_{ber.}$ = 1.483 g cm^{-3}; μ (MoK$_\alpha$) = 2.398 mm^{-1}, F(000) = 5728, 113 953 reflections ($2\theta_{max}$ = 50°) measured (42 874 unique, R_{int} = 0.027), R(for $I > 2\sigma(I)$) = 0.0760, w$R2$(all data) = 0.2060, GOF = 1.074 for 1241 parameters and 3078 restraints, largest diff. peak and hole 2.854 e Å^{-3} (triflate)/−1.555 e Å^{-3}; a semi-empirical absorption correction was applied, max./min. transmission 0.4305/0.3258, absolute structure parameter x = 0.06(1).[15b]

The structure shows unequivocally the constitution, conformation and configuration of the square, with probable disorder in the side chains, the phenyl groups, the anions and the solvent and a large void (>1200 Å^3), which seems to contain several highly disordered and unidentifiable solvent molecules. Due to the bad quality of the data, caused by this disorder, only the Pt, P and six of the eight S-atoms were refined anisotropically. Restraints for geometry and displacement parameters were used to refine the sidechains, the anions and the solvent molecules. The phenyl groups were refined as a rigid group using a constrained model (AFIX 66). The disorder of the anions, side chains, phenyl groups, and solvent molecules could not be resolved. Due to this problem, there are a also number of short intermolecular H–H, but also X–Y contacts, and NH-groups without acceptor.

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