Binuclear and polynuclear transition metal complexes with macrocyclic ligands 4.* New polydentate azomethine ligands based on 2,5-diformylpyrrole and 2,6-diformylpyridine

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The reactions of 2,5-diformylpyrrole (1) and 2,6-diformylpyridine (2) with propane-1,3diamine afforded new macrocyclic Schiff's bases 5 and 6, respectively. Their structures were established by NMR spectroscopy and mass spectrometry. Binuclear copper(II) and nickel(II) complexes with ligand 5 were synthesized. Pentadentate Schiff's base, *viz.*, 2,6-bis[(2-aminophenylimino)methyl]pyridine, was prepared by demetallation of its complex with Cd(ClO₄)₂ using Na₂S. In solutions, the latter Schiff's base is quantitatively transformed into 2,6-bis(benzoimidazolyl)pyridine under the action of atmospheric oxygen or other mild oxidizing agents.

Key words: macrocyclic ligands, Schiff's bases, NMR spectroscopy, mass spectrometry, MALDI-TOF, ESI-MS.

Macrocyclic Schiff's bases generated from diamines and α, α' -dicarbonyl derivatives of pyrrole and pyridine were relatively poorly studied compared to macrocycles based on 2,6-dicarbonyl derivatives of 4-substituted phenols. Template syntheses in the presence of metal ions allow one to prepare complexes with macrocyclic ligands. However, the preparation of free ligands often presents difficulties.

Generally, the reactions of 2,5-diformylpyrrole (1) or 2,6-diformylpyridine (2) with aliphatic diamines in the absence of metal ions afford mixtures of oligomeric condensation products.² However, the reactions of 1 with

1,4-diaminobutan-2-ol³ and diethylenetriamine⁴ gave rise to macrocyclic [2+2]-condensation products. The reaction of **1** with ethylenediamine produced compound **3**, which was generated due to the addition of a water molecule to the [2+2]-macrocycle⁵ (as a rule, these reactions are carried out in the presence of catalytic amounts of acids, for ex-



ample, of HNO₃ or HCl). 2,6-Diformylpyridine (**2**) and 2,6-diacetylpyridine form [2+2]-macrocyclic Schiff's bases with diamines containing additional heteroatoms in the aliphatic chain.^{4,6,7}

* For Part 3, see Ref. 1.

We found that condensation of compounds 1 and 2 with propane-1,3-diamine (4) using dry MeCN as the solvent in the absence of acid gave rise to macrocycles 5 and 6, respectively, in good yields (Scheme 1).

Within approximately 2 h after the completion of the slow addition of the dialdehyde to a very dilute solution of compound 4 in dry MeCN, white small crystals of the macrocycles began to precipitate. Crystals of compound 5 are very moisture-sensitive and deliquesce on storage in air. When organic solvents (THF, CH₂Cl₂, or CHCl₃) were not sufficiently dried, their removal from solutions of compound 5 by distillation resulted in isolation of 5 as a viscous oil, which solidified on drying under high vacuum. The structure of compound 5 was confirmed by ¹H and ¹³C NMR spectroscopy and ESI mass spectrometry. The ¹H NMR spectrum (CDCl₃) has only four broadened signals at δ 1.98, 3.60, 6.43, and 8.04 with the integral intensity ratio of 4:8:4:4 corresponding to the CH atoms. The signal of the N–H protons of the pyrrole fragment is broadened to an extent that it is unobservable. Apparently, broadening of the NMR signals is attributed to exchange processes associated with rather rapid interconversions of several energetically similar conformers of the macrocycle. Studies of these processes by dynamic NMR spectroscopy are currently underway.

Unlike macrocycle **5**, compound **6** is not highly hygroscopic, and no broadening of the signals is observed in its NMR spectra. In weakly acidic aqueous solutions, both

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Reagents and conditions: *i*. MeCN, 20 °C, 24 h; *ii*. MeCN, 20 °C, 48 h.

macrocycles **5** and **6** are readily hydrolyzed to give the starting dialdehydes and diamine **4**.

Macrocycle **5** reacts with copper(II) and nickel(II) acetates in an $CHCl_3$ —MeOH mixture to form binuclear complexes **7** and **8**, respectively (Scheme 2).

Scheme 2



Reagents and conditions: *i*. M(OAc)₂, CHCl₃+MeOH, 20 °C, 24 h.

Complexes 7 and 8 were obtained as bright-green and olivine-colored crystalline compounds, respectively. These compounds are readily soluble in water and MeOH, moderately soluble in THF, poorly soluble in $CHCl_3$ and

 CH_2Cl_2 , and insoluble in nonpolar organic solvents, whereas the binuclear nickel complex with a macrocycle based on diformylpyrrole and *o*-phenylenediamine, which we have studied earlier,⁸ is very poorly soluble in most of organic solvents.

It is known that the reaction of 2,6-diacetylpyridine with 1,2-diaminobenzene or 1,2-diaminoethane in the presence of $Cd(ClO_4)_2$ affords cadmium complexes with polydentate Schiff's bases 9 as a result of [1+2]-condensation of the starting reagents.⁹



$$H_2N X NH_2 = H_2N (a), H_2N (b)$$

We succeeded in preparing free polydentate Schiff's base **10** in 98% yield by the reaction of sodium sulfide with complex **9a**. It should be noted that compound **10** cannot be synthesized by direct condensation of dialdehyde **2** with 1,2-diaminobenzene. Products of [1+2]-condensation of dicarbonyl compounds with 1,2-diaminobenzene as free ligands have previously been unknown. The reaction of complex **9b** with Na₂S produced 2,6-diformylpyridine (**2**) and ethylenediamine due, apparently, to the fact that [1+2]-Schiff's base formed as an intermediate has lower hydrolytic stability under these conditions, which is typical of azomethines based on aliphatic amines (Scheme 3).



Pentadentate ligand **10** contains three types of N-donor centers, which is of particular interest for the synthesis of binuclear metal complexes and for its further use as a building block in the synthesis of unsymmetrical macrocyclic ligands.

Compound **10** was prepared as a bright-yellow compound, which is readily soluble in CHCl₃, CH₂Cl₂, and AcOEt and less soluble in MeOH and MeCN (~1.25 g L⁻¹). The ¹H NMR spectrum of compound **10** in CD₃CN has an AMPX system with signals at δ 6.42 (H(3)), 6.55 (H(2)), 6.85 (H(4)), and 7.01 (H(5)) belonging to the aromatic protons, a broad signal of the protons of the amino groups at δ 4.46, an A₂X system with signals at δ 7.71 (H(8)) and 8.12 (H(7)) belonging to the protons of the pyridine residue, and a singlet of the protons of the imino groups at δ 8.50. The UV spectrum of **10** shows two absorption maxima at 312 nm (ϵ = 15000) and 408 nm (ϵ = 3500).

Compound **10** is storage-stable in the solid state but it is gradually oxidized in solutions in the presence of atmospheric oxygen, particularly, in weakly acidic media, to give 2,6-bis(benzoimidazolyl)pyridine (**11**) described earlier.^{**10**} The latter is generated in quantitative yield upon stirring of a solution of compound **10** in CHCl₃ in air in the presence of silica gel or under the action of I₂ in MeOH (Scheme 4).

Scheme 4



Reagents and conditions: i. 1) I₂, MeOH, 20 °C, 12 h; 2) NaOH.

Earlier, condensation of 1,2-diaminobenzenes with 2,6-diformylpyridine (2) (in the presence of lanthanide salts¹⁰) and 2,6-diformylphenols (refluxing in EtOH)^{1,11} afforded bis-benzoimidazole derivatives as a result of intramolecular cyclization of Schiff's bases (analogs of ligand **10**) that formed in the first step.

The reaction of compound 10 with $Cu(OAc)_2$ in a MeCN—MeOH mixture produced a dark-red precipitate. According to the mass-spectrometric data, this

precipitate is the complex $11 \cdot \text{Cu(OAc)}_2$ (12). The MALDI-TOF spectrum of 12 has two peaks at m/z 311.7 and 373.7 corresponding to the $[L + H]^+$ and $[LCu - H]^+$ ions, respectively. The reaction of Na₂S with a methanolic solution of complex 12 led to recovery of the starting ligand 11 in 85% yield.

The formation of benzoimidazoles from Schiff's bases in the presence of copper(11) salts as well as of other oxidizing agents has been described many times.¹² Earlier, it has been demonstrated⁹ that refluxing of a solution of cadmium complex **9a** in MeOH with an excess of Ni(ClO₄)₂ followed by prolonged storage in air afforded a compound, to which the structure of a nickel complex with ligand **11** was assigned based on analysis of the IR and UV spectra.

Experimental

The UV-Vis spectra were recorded on a Specord-UV spectrophotometer in the region of 200–900 nm. The IR spectra (in KBr pellets or Nujol mulls) were measured on a Specord-M400 spectrophotometer in the region of 400–4000 cm⁻¹. The ¹H and ¹³C NMR spectra were recorded on a Bruker DPX-300 instrument (300 MHz) with Me₄Si as the internal standard. The mass spectra of the positive ions were obtained on Kratos MS-890 (70 eV), Finnigan MAT LCQ (ESI), and Bruker MALDI-TOF Reflex 3 (UV laser, $\lambda = 337$ nm) instruments. The starting dialdehydes, *viz.*, 2,5-diformylpyrrole¹³ and 2,6-diformylpyridine,¹⁴ and complex **9a** ⁹ were prepared according to known procedures. The constants of compounds **9a** and **11** described earlier are identical with the published data.⁹

3,7,14,18,23,24-Hexaazatricyclo[18.2.1.19,12]tetracosa-2,7,9,11,13,18,20,22-octaene (5). A solution of 2,5-diformylpyrrole (1) (200 mg, 1.62 mmol) in dry MeCN (10 mL) was added dropwise to a solution of propane-1,3-diamine (4) (120 mg, 135 µL, 1.62 mmol) in dry MeCN (30 mL) for 10 min and then the reaction mixture was stirred for 24 h. The solution was carefully decanted from the colorless finely crystalline precipitate that formed (the compound is very hygroscopic in solution). The precipitate was dried in vacuo and compound 5 was recrystallized from a mixture of dry MeCN and CHCl₃ (~1 : 1). The yield of compound 5 was 170 mg (66%), m.p. 127 °C. Found (%): C, 66.80; H, 7.02; N, 26.18. C₁₈H₂₂N₆. Calculated (%): C, 67.06; H, 6.88; N, 26.07. MS (EI, 70 eV), m/z (I_{rel} (%)): 322.4 [M]⁺ (5.05). ¹H NMR (CDCl₃), δ : 1.98 (br.s, 4 H); 3.60 (br.s, 8 H); 6.43 (br.s, 4 H); 8.04 (br.s, 4 H). ¹³C NMR (CDCl₃), δ: 32.4, 58.8, 114.3, 132.5, 151.7. IR (KBr), v/cm^{-1} : 740, 950, 1020, 1160, 1260, 1440, 1620, 3420. UV (6.21 \cdot 10⁻⁴ M solution in an EtOH-CH₂Cl₂ mixture, 1 : 1), λ_{max}/nm (ϵ): 243 (5600), 304 (18500), 322 (22200), 334 (4800).

3,7,15,19,25,26-Hexaazatricyclo[19.3.1.1^{9,13}]hexacosa-2,7,9,11,13(26),14,19,21(25),22,24-decaene (6). A solution of 2,6-diformylpyridine (2) (100 mg, 0.74 mmol) in dry MeCN (10 mL) was added dropwise to a solution of diamine 4 (70 μ L, 0.74 mmol) in dry MeCN (30 mL) for 2 h. The reaction mixture was stirred for 48 h. The white finely crystalline precipitate that formed was filtered off and twice recrystallized from a mixture of anhydrous MeCN and CHCl₃ (1 : 1). Ligand **6** was obtained in a yield of 80 mg (62%), m.p. 165 °C. Found (%): C, 69.25; H, 6.55; N, 24.10. $C_{20}H_{22}N_6$. Calculated (%): C, 69.34; H, 6.40; N, 24.26. MS (EI, 70 eV), m/z (I_{rel} (%)): 346.4 [M]⁺ (15.38). ¹H NMR (CDCl₃), δ : 2.15 (q, 4 H, J = 6.6 Hz); 3.80 (t, 8 H, J = 6.6 Hz); 7.78 (t, 2 H, J = 7.8 Hz); 8.12 (d, 4 H, J = 7.5 Hz); 8.44 (s, 4 H). IR (Nujol mulls), v/cm⁻¹: 820, 1340, 1380, 1460, 1590, 1650. UV (5.78 · 10⁻⁴ *M* solution in an EtOH—CH₂Cl₂ mixture, 1 : 1), λ_{max}/nm (ϵ): 243 (8800), 277 (5450).

Complex 7. A cooled (-10 °C) solution of $Cu(OAc)_2 \cdot H_2O$ (248 mg, 1.24 mmol) in MeOH (20 mL) was added to a solution of ligand 5 (200 mg, 0.62 mmol) in CHCl₃ (30 mL) at -10 °C. The reaction mixture was stirred at ~20 °C for 24 h. The solvent was removed on a rotary evaporator to obtain a green powder, which was placed on a filter and washed one time with warm CHCl₃. The residue was dried in vacuo and recrystallized from a MeOH-Et₂O mixture to prepare complex $7 \cdot Cu(OAc)_2$ in a yield of 316 mg (68%). Found (%): C, 41.21; H, 4.15; N, 12.05; Cu, 25.33. C₂₆H₃₂Cu₃N₆O₈. Calculated (%): C, 41.79; H, 4.32; N, 11.25; Cu, 25.51. Upon heating to 350 °C, the compound gradually darkened and decomposed. MS (MALDI-TOF, m/z): 445.7 $[(5 - 2 \text{ H})Cu_2]^+$. UV (2.67 · 10⁻⁴ M solution in an EtOH-CH₂Cl₂ mixture, 1 : 1), λ_{max}/nm (ϵ): 243 (18000), 266 (15000), 364 (14750). IR (Nujol mulls), v/cm⁻¹: 1590, 1460, 1390, 1050, 810.

Complex 8. A cooled (-10 °C) solution of Ni(OAc)₂ · 4H₂O (307 mg, 1.24 mmol) in MeOH (20 mL) was added to a solution of ligand 5 (200 mg, 0.62 mmol) in CHCl₃ (30 mL) at -10 °C. The reaction mixture was stirred at ~20 °C for one day. The solvent was removed on a rotary evaporator. The olivine-colored powder that formed was placed on a filter and washed one time with warm CHCl₃. The residue was dried *in vacuo* and recrystallized from a MeOH-Et₂O mixture. Compound **8** was obtained in a yield of 237 mg (69%). Upon heating to 350 °C, the compound gradually darkened and decomposed. Found (%): C, 47.31; H, 4.96; N, 15.33. C₂₂H₂₆N₆Ni₂O₄. Calculated (%): C, 47.54; H, 4.71; N, 15.12. MS (ESI, *m/z*): 454.0, [(**5** - 2 H)Ni₂OH]⁺; 379.1, [(**5** - H)Ni₁- H]⁺; 398.1 [(**5** - H)Ni H₂O]⁺; 379.1, [(**5** - H)Ni₁- H]⁺; 398.1 [(**5** - H)Ni H₂O]⁺; 379.1, [(**5** - H)Ni₁- H]⁺; 398.1

Complex 9a.⁹ 2,6-Diformylpyridine (2) (1 g, 7.4 mmol) and Cd(ClO₄)₂•6H₂O (3.68 g, 8.78 mmol) were successively dissolved in anhydrous MeOH (40 mL) and then a solution of *o*-phenylenediamine (2.43 g, 22.5 mmol) in anhydrous MeOH (20 mL) was rapidly added. The reaction mixture was refluxed for 40 min and cooled to -20 °C. The orange crystalline precipitate that formed was filtered off. Complex **9a** was prepared in a yield of 4.78 g (87%). Found (%): C, 41.0; H, 3.62; N, 13.71. C₂₅H₂₅CdCl₂N₇O₈. Calculated (%): C, 40.86; H, 3.43; N, 13.34.

2,6-Bis{[(2-aminophenyl)imino]methyl}pyridine (10). Water (70 mL), MeOH (10 mL), and crystalline Na₂S (5 g) were added to a suspension of complex **9a** (1 g) in CH₂Cl₂ (70 mL). The resulting suspension was thoroughly stirred for 5 h. The upper aqueous layer into which CdS gradually went as a suspension was decanted and a new portion of water was added. Then Na₂S (5 g) was added and the mixture was stirred for one day. The organic layer was separated, washed three times with water, and dried over K₂CO₃. The solvent was distilled off on a rotary evaporator. Ligand **10** was obtained in a yield of 420 mg (98%), m.p. 107 °C. Found (%): C, 72.16; H, 5.56; N, 21.84. C₁₉H₁₇N₅. Calculated (%): C, 72.36; H, 5.43; N, 22.21. ¹H NMR (CD₃CN), δ : 4.46 (br.s, 4 H, H(1)); 6.42 (dt, 2 H, H(3), ³J =

6.6 Hz, ${}^{4}J$ = 3.3 Hz); 6.55 (dd, 2 H, H(2), ${}^{3}J$ = 7.2 Hz, ${}^{4}J$ = 1.2 Hz); 6.85 (dt, 2 H, H(4), ${}^{3}J$ = 6.6 Hz, ${}^{4}J$ = 3.3 Hz); 7.01 (dd, 2 H, H(5), ${}^{3}J$ = 7.2 Hz, ${}^{4}J$ = 1.2 Hz); 7.71 (t, 1 H, H(8), $J_{7,8}$ = 7.8 Hz); 8.12 (d, 2 H, H(7), $J_{8,7}$ = 7.8 Hz); 8.50 (s, 2 H, H(6)). 13 C NMR (DMSO-d₆), δ: 115.0; 116.2; 117.1; 122.5; 128.7; 133.7; 137.5; 144.7; 154.7; 155.1. IR (Nujol mulls), v/cm⁻¹: 740, 810, 950, 1000, 1150, 1260, 1310, 1380, 1460, 1610. UV (6.349 · 10⁻⁴ *M* solution in EtOH), λ_{max}/nm (ε): 312 (15000), 408 (3500).

Reaction of compound 10 with iodine. Iodine (1 equiv., 80.5 mg, 0.317 mmol) was added to a solution of ligand **10** (100 mg, 0.317 mmol) in a mixture of CH₂Cl₂ (10 mL) and MeOH (15 mL). The reaction solution was stirred for 5 h and then NaOH (25.4 mg) was added. The solvent was removed on a rotary evaporator. The organic layer was extracted with MeOH and the extract was concentrated. The residue was dried *in vacuo*. A pale-yellow powder of 2,6-bis(benzoimidazolyl)pyridine **11** was obtained in a yield of 92 mg (94%). ¹H NMR (DMSO-d₆), 8: 7.32 and 7.76 (both m, 4 H each, 4 CH); 8.15 (t, 1 H, J = 7.8 Hz); 8.35 (d, 2 H, J = 7.8 Hz); 12.98 (s, 2 H).

Reaction of compound 10 with Cu(OAc)₂. A solution of Cu(OAc)₂·H₂O (190.4 mg, 0.95 mmol) in MeOH (10 mL) was rapidly added to a cooled (-10 °C) solution of compound 7 (300 mg, 0.95 mmol) in MeCN (10 mL). The reaction mixture was stirred for 24 h and the solvent was removed to prepare a dark-red powder, which was washed with MeCN and Et₂O, recrystallized by diffusion of Et₂O into a solution of the compound in MeOH, and dried *in vacuo*. Complex **12** was obtained in a yield of 288 mg (67%). MS (MALDI-TOF, *m/z*): 311.7 [L + H]⁺, 373.7 [LCu - H]⁺. UV (4.43 \cdot 10⁻⁴ M solution in EtOH), λ_{max}/nm (ϵ): 332 (22600).

Sodium sulfide (100 mg) was added to a solution of compound **12** (200 mg) in MeOH (50 mL). The reaction mixture was stirred for 30 min and filtered. The solvent was removed on a rotary evaporator. The residue was washed on a filter with CHCl₃ and dried in air. Compound **11** was prepared in a yield of 75 mg (85%). The ¹H NMR spectroscopic data for **12** are identical to those published in the literature.⁹

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