

published by Ural Federal University eISSN 2411-1414 <u>chimicatechnoacta.ru</u> ARTICLE 2025, vol. 12(2), No. 12217 DOI: <u>10.15826/chimtech.2025.12.2.17</u>

Copper(II) complexes with fluorinated 5-aryl-2,2'bipyridine-6(6')-carboxylic acid tridentate ligands

Timofey D. Moseev ^a, Mikhail V. Varaksin ^{ab} ^{*}, Alexey P. Krinochkin ^{ab}, Maria I. Valieva ^{ab}, Ekaterina A. Kudryashova ^a, Yulia M. Sayfutdinova ^a, Anastasiya V. Rybakova ^c, Dmitry S. Kopchuk ^{ab}, Grigory V. Zyryanov ^{ab}, Youcef Ballou ^a, Pavel A. Slepukhin ^{ab}, Vasiliy S. Gaviko ^{ad}, Valery N. Charushin ^{ab}, Oleg N. Chupakhin ^{ab}

- a: Institute of Chemical Engineering, Ural Federal University, Ekaterinburg 620062, Russia
- b: I.Ya. Postovsky Institute of Organic Synthesis, Ural Branch of the RAS, Ekaterinburg 620066, Russia
- c: South Ural State University, Chelyabinsk 454080, Russia
- d: Institute of Physics of Metals, Ural Branch of the RAS, Ekaterinburg 620108, Russia
- * Corresponding author: m.v.varaksin@urfu.ru

Abstract

Three Cu(II) complexes containing (poly)fluorine ligands based on 5-aryl-2,2'-bipyridine-6(6')-carboxylic acids have been synthesized for the first time. These complexes belong to either triclinic (P-1) or orthorhombic (Iba2) crystal systems. The packing of molecules in Cu(II) complexes, confirmed by Xray diffraction (XRD) structural analysis, seems to be due to the effect of fluorine atoms involved in the formation of hydrogen bonds or intermolecular short contacts of type C-F... π , as well as the influence of the crystallization solvent molecules. The developed coordination compounds could be of interest in the design of pharmacologically active substances, chemosensors, and catalytic systems.

Key findings

- Synthesis of fluorinated ligands and their conversion to copper(II) complexes.
- Copper(II) complexes with distorted square pyramidal and octahedral coordination geometries and typical bond lengths.
- Supramolecular interactions, including hydrogen bonding and π - π stacking, as driving forces for the crystal packing of the complexes.

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Accompanying information

Article history Received: 28.02.25 Revised: 06.04.25 Accepted: 11.04.25 Available online: 28.04.25

Keywords

2,2'-bipyridine-6-carboxylic acids, (poly)fluorine-containing compounds, copper(II) complexes, XRD analysis, nucleophilic substitution of hydrogen, 1,2,4-triazines

Funding

This work was supported by the Russian Science Foundation (20-73-10077, https://www.rscf.ru/en/project/20-73-10077/).

Supplementary information

Supplementary materials: **CREAD**

Transparent peer review: **CREAD**

Sustainable Development Goals



1. Introduction

Cu(II) complexes of 2,2'-bipyridines and their condensed analogues are known to be of interest in the design of pharmacologically active compounds with antitumor [1, 2] or antibacterial [3] activity. Besides, these compounds are also widely used as catalysts [4] and agents for the generation of reactive oxygen species (ROS) for photodynamic therapy [5]. Moreover, complexes of 5-(het)aryl-2,2'-bipyridines are known to demonstrate antimicrobial [6] and chemosensory [7] properties, e.g., for the determination of halogen ions [8]. At the same time, tridentate N^N^O ligands based on 2,2'- bipyridine-6-carboxylic acids are currently represented by only a few known examples [9–12]. It is important to note that the targeted modification of ligands with various electronegative groups, in particular (poly)fluoroaromatic ones, allows one to tune their physicochemical, luminescent, and redox properties, and also directly affects their crystal structure and spatial packing [13–17]. Thus, this paper deals with the study of (poly)fluorinated 2,2'-bipyridine-6-carboxylic acids as ligands for copper(II) cations, as well as the effect of fluorine atoms on the structure and properties of the corresponding complexes.



2. Experimental part

All reagents were purchased from Shanghai Macklin Biochemical Technology and used without further purification. NMR spectra were recorded on a Bruker Avance-400 and Bruker Avance-600 spectrometers at 298 K, digital resolution \pm 0.01 ppm, using TMS as internal standard for ¹H and CFCl₃ for ¹⁹F spectra. Elemental analyses were performed on a PE 2400 II CHN-analyzer (Perkin Elmer). Mass spectrometry data of compounds **2** and **3** were acquired on a Shimadzu GCMS-QP2010 Ultra mass-spectrometer with electron ionization; the mass spectrometry data of the other compounds were acquired using an Agilent 6545 Q-TOF LC-MS with electrospray ionization.

The X-ray diffraction analysis of compound Cu•6A was carried out on an automatic 4-circle Xcalibur 3 X-ray diffractometer with a CCD detector using a standard technique (graphite monochromator, Mo Kα radiation, and ω scanning in 1° increments at T = 295(2) K). An empirical correction for absorption was applied. The X-ray diffraction analysis of complexes Cu+5 and Cu+6 was performed on an automatic Rigaku XtaLAB Synergy four-circle diffractometer with a HyPix-6000HE CCD detector and a PhotonJet X-ray source according to a standard procedure (MoKα radiation, graphite monochromator, and ω scanning in 1° increments) at T = 295(2) K. An empirical correction for absorption was applied. The measured reflection data were indexed, integrated, and scaled using the CrysAlisPro software package [18]. The structures were deciphered by the internal phasing method according to the SHELXT program [19] and refined by the least squares method for F² using the SHELXL program [20]. The decoding and refinement of the structure were carried out in the Olex2 software shell [21]. Nonhydrogen atoms were refined in the anisotropic approximation. Hydrogen atoms at oxygen atoms were identified from the Fourier difference series. All other hydrogen atoms were placed in calculated positions in accordance with stereochemical criteria and refined according to the rider scheme. The results of X-ray diffraction analysis are registered in the Cambridge Structural Database under the CCDC numbers 2421972 (for Cu·5), 2435014 (for Cu·6) and 2421949 (for Cu•6A). This data is freely available and can be requested at https://www.ccdc.cam.ac.uk/.

The X-ray powder diffraction data for complex **Cu-6** was collected on a «Empyrean» high-resolution X-ray diffractometer in copper filtered radiation. Processing and calculation of parameters was carried out using the software package HighScore Plus 4.1.

The starting 1,2,4-triazine **1** [22] and 2,2'-bipyridine-6carbonitrile **6** [23] were synthesized as described in the literature.

Compounds **2** and **3** were prepared according to previously reported methodology [24] using pentafluorobenzene (1 mmol) and methyl 6-(6-phenyl-1,2,4-triazin-3-yl)picolinate **1** (1 mmol).

Methyl 6-(5-(perfluorophenyl)-6-phenyl-4,5-dihydro-1,2,4-triazin-3-yl)picolinate (2). M.p. 178-180 °C. Yield 345 mg (0.75 mmol, 75%). NMR ¹H (600 MHz, CDCl₃, δ, ppm): 4.03 (s, 3H, Me), 6.39 (s, 1H, C_{sp3}-H), 7.33-7.38 (*m*, 3H, Ph), 7.65–7.71 (*m*, 2H, Ph), 7.94 (*dd*, 1H, *J* = 7.8, 7.8 Hz, H-4), 8.22 and 8.30 (both d, 1H, ³J 7.8 Hz, H-6 and H-3), 10.42 (br. *s*, 1H, NH). NMR ¹⁹F (565 MHz, CDCl₃, δ, ppm): (-161.50)-(-161.39) (m, 2F), (-154.28)-(-154.18) (m, 1F), (-142.74)-(-142.51) (m, 2F). NMR ^{13}C (151 MHz, CDCl3, $\delta,$ ppm): 47.1, 52.9, 115.8-115.4 (*m*), 125.6, 126.9, 128.8, 129.9, 130.9, 132.5, 134.3, 137.7 (dm, J = 250.3 Hz), 138.2, 138.6, 140.9 (dm, J = 250.6 Hz), 145.5 (dm, J = 249.5 Hz), 146.7, 148.4, 149.0, 165.0, 167.8. MS (EI, *m/z*): found 460; calculated 460 [M⁺]. Found, %: C 57.47, H 2.91, N 12.22. For $C_{22}H_{13}F_5N_4O_2$ calculated, %: C 57.40, H 2.85, N 12.17, O 6.95, F 20.63.

Methyl 6-(5-(perfluorophenyl)-6-phenyl-1,2,4-triazin-3-yl)picolinate (3). M.p. 161-163 °C. Yield 338 mg (0.74 mmol, 98%). NMR ¹H (600 MHz, CDCl₃, δ, ppm): 4.04 (s, 3H, Me), 7.43-7.47 (m, 2H, Ph), 7.49-7.54 (m, 1H, Ph), 7.57-7.61 (m, 2H, Ph), 8.14 (dd, 1H, ³J 7.8, 7.8 Hz, H-4), 8.36 and 8.23 (both dd, 1H, ³J 7.8 Hz, ⁴J 0.8 Hz, H-6 and H-3). NMR ¹⁹F (565 MHz, CDCl₃, δ , ppm): (-159.73)-(-159.62) (m, 2F), (-149.49)-(-149.41) (m, 1F), (-139.39)-(-139.31) (m, 2F). NMR ^{13}C (151 MHz, CDCl3, $\delta,$ ppm): 53.1, 111.7-111.4 (m), 128.5, 128.8, 129.0, 130.9, 132.5, 133.4, 137.8 (dm, J = 252.5 Hz), 138.5, 142.7 (dm, *J* = 250.7 Hz), 144.5 (dm, *J* = 252.5 Hz), 146.8, 149.1, 152.3, 158.5, 160.7, 165.4, 167.8. MS (EI, *m/z*): found 458; calculated 458 [M⁺]. Found, %: C 57.71, H 2.45, N 12.26. For C₂₂H₁₁F₅N₄O₂ calculated, %: C 57.65, H 2.42, N 12.22, O 6.98, F 20.72.

Methyl 6'-(perfluorophenyl)-5'-phenyl-2,2'-bipyridine-6-carboxylate (4). 105 mg (0.23 mmol) of 1,2,4-triazine 3 was suspended in 25 mL of 1,2-dichlorobenzene, 0.12 mL (1.15 mmol) of 2,5-norbornadiene was added to the suspension, and the resulting mixture was stirred under reflux for 27 h (with the addition of 0.06 mL of 2,5-norbornadiene every 9 h). The solvent was removed under reduced pressure. The product was isolated by column chromatography (CH₂Cl₂ as eluent, Rf 0.4). An analytical sample was obtained by recrystallization from MeCN. Yield 83 mg (0.18 mmol, 79%). NMR ¹H (400 MHz, CDCl₃, δ, ppm): 4.06 (s, 3H, OMe), 7.19-7.24 (m, 2H, Ph), 7.31-7.36 (m, 3H, Ph), 7.93-7.99 (m, 2H, H-3', H-4), 8.16 and 8.60 (both dd, 1H, ³J = 7.6 Hz, ${}^{4}J$ = 0.8 Hz, H-3 and H-5), 8.71 (d, 1H, ${}^{3}J$ = 8.0 Hz, H-4'). NMR ¹⁹F (376 MHz, CDCl₃, δ, ppm): (-162.20)-(-160.00) (m, 2F), -154.19 (dd, J = 20.4 Hz, 20.4 Hz, 1F), (-140.85)-(-140.70) (m, 2F). MS (ESI, m/z (Irel, %)): found 457.10; calculated 457.10 [M+H]⁺. Found, %: C 63.08, H 2.93, N 6.22. For $C_{24}H_{13}F_5N_2O_2$ calculated, %: C 63.16, H 2.87, N 6.14.

Sodium 6'-(perfluorophenyl)-5'-phenyl-2,2'-bipyridine-6-carboxylate (5). 91 mg (0.20 mmol) of ester **4** were suspended in 30 mL of ethanol, and then the resulting suspension was heated until a solution was formed. An equimolar amount of NaOH (8.0 mg, 0.20 mmol) was added to the solution cooled to room temperature, and the resulting mixture was kept at room temperature for 12 h. The solvent was then removed under reduced pressure. The resulting product was used in the next step without further purification. Yield 83 mg (0.18 mmol, 90%). NMR ¹H (400 MHz, CD₃OD, δ , ppm): 7.26–7.31 (m, 2H, Ph), 7.34–7.42 (m, 3H, Ph), 7.96 (dd, 1H, ³J 7.6, 7.6 Hz, H-4), 8.06-8.11 (m, 2H, H-3', H-3), 8.44 (dd, 1H, ³J 8.0, ⁴J 1.0 Hz, H-5), 8.96 (d, 1H, ³J 8.0 Hz, H-4'). NMR ¹⁹F (376 MHz, CD₃OD, δ , ppm): (-165.45)-(-165.25) (m, 2F), -157.57 (dd, *J* = 19.0, 19.0 Hz, 1F), (-143.20)-(-143.15) (m, 2F). MS (ESI, *m/z* (I_{rel}, %)): found 441.07; calculated 441.07 [M-Na]⁻.

Complex Cu-5. A solution of 31 mg (0.18 mmol) CuCl₂•2H₂O in 15 mL of ethanol was added to a solution of 70 mg (0.15 mmol) of sodium salt **5** in 25 mL of ethanol. The resulting reaction mixture was stirred at 60 °C for 10 h. After cooling to rt, the solution was concentrated under reduced pressure, the resulting precipitate was filtered, washed with ethanol and dried. A single crystal of compound **Cu-5** suitable for X-ray diffraction analysis was obtained by slow evaporation of its water-methanol solution (solvent ratio 1:1). Yield 47 mg (0.05 mmol, 66%). IR, v/cm⁻¹: 1645 (CO). MS (ESI, *m/z* (Irel, %)): found 946.07; calculated 946.07 [M+H]⁺. Found, %: C 58.26, H 2.01, N 6.14. For C₄₆H₂₀CuF₁₀N₄O₄ calculated, %: C 58.39, H 2.13, N 5.92. Crystallographic data are represented in Table S1. CCDC registration code 2421972.

Complex Cu-6. A solution of 32 mg (0.19 mmol) CuCl₂•2H₂O in 15 mL of ethanol was added to a suspension of 50 mg (0.16 mmol) of 2,2'-bipyridine **6** in 25 mL of ethanol. The resulting reaction mixture was stirred at 60 0 C for 10 h. After cooling to rt, the solution was concentrated under reduced pressure, the resulting crude precipitate was filtered, washed with ethanol and dried. A single crystal of compound **Cu-6** suitable for X-ray diffraction analysis was obtained by recrystallization (EtOH:MeOH:water, 7:2:1). Yield 45 mg (0.05 mmol, 61%). IR, v/cm⁻¹: 1674 (CO). MS (ESI, *m/z* (I_{rel}, %)): found 863.01; calculated 863.01 [M+H]⁺. Found, %: C 54.23, H 3.79, N 6.16. For C₄₀H₂₈Cl₂Cu₂F₂N₄O₄•2MeOH calculated, %: C 54.31, H 3.91, N 6.03. Crystallographic data are represented in Table S1. CCDC registration code 2435014.

The crystals of complex **Cu-6A** suitable for X-ray diffraction analysis were obtained by low evaporation of the water-methanol (1:1) solution of the crude precipitate. ESI-MS, m/z (I_{rel}, %): found 863.01; calculated 863.01 [M+H]⁺. Crystallographic data are represented in Table S1. CCDC registration code 2421949.

3. Results and Discussion

To study the effect of fluoroaromatic groups on the structural features of the complexes, two 2,2'-bipyridine ligands containing one (**6**) and five (**5**) fluorine atoms were synthesized (Scheme 1). For this purpose, the "1,2,4-triazine" methodology [25, 26] for the synthesis of (oligo)pyridines was used. The reason for the application of this approach was due to the possibility of convenient functionalization of the triazine cycle using nucleophilic hydrogen substitution reactions (S_N^H) following the basic principles of green chemistry [27-29]. Thus, previously described [22] pyridyltriazine 1 bearing an ester group at position C6 of the 2pyridyl fragment, being a precursor of the carboxyl group, was used as the starting compound. The methodology of nucleophilic substitution of hydrogen (S_N^H) was employed herein to incorporate a pentafluorophenyl substituent into position C5 of the triazine, in accordance with the previously outlined procedure [24]. It is important to note that the presence of the ester group has been found not to result in difficulties for this transformation. Thus, at the first stage, stable σ^{H} -adduct 2 was synthesized in 75% yield as a result of interaction with pentafluorophenyl lithium, obtained in situ, under anhydrous conditions. In the case of functionalization of 1,2,4-triazines by this methodology, the formation of stable σ^{H} -adducts is typical [30, 31]. At the next stage, DDQ (2,3-dichloro-4,5-dicyanobenzoquinone) was utilized as an oxidizing agent for its aromatization, with an almost quantitative yield being achieved. Subsequent conversion of the triazine ring of compound 3 into a pyridine one by reaction with 2,5-norbornadiene and alkaline hydrolysis of the ester group of 4 led to the target ligand as the sodium salt 5. Complex Cu•5 was obtained by reaction of 5 with copper(II) chloride in ethanol. The corresponding single crystals of Cu•5 for X-ray diffraction analysis (XRD) were obtained by slow evaporation of their solutions in a mixture of methanol and water (1:1).

Meanwhile, to produce the copper complex **Cu-6** containing one fluorine atom, the described earlier [9, 23] 2,2'bipyridine-6-carbonitrile **6** was used (Scheme 2). This compound was also obtained by a series of S_N^H and Boger reactions [32], and in the latter case 1-morpholinocyclopentene was exploited as a dienophile. Thus, the hydrolysis of the cyano group was found to take place as a result of boiling the reaction mixture in aqueous ethanol in the presence of copper(II) chloride, with the target copper complex forming in one stage [9] (Scheme 2). It is worth noting that this approach significantly simplifies the synthesis of the corresponding acids, as compared with the usual method for hydrolysis of the cyano group that, for such compounds, requires prolonged heating in 50% sulfuric acid [23].

In particular, this approach was utilized in the preparation of the corresponding Ln(III) complexes of 2,2'-bipyridine-6-carboxylic acids, when the possibility of hydrolysis under standard conditions was considerably complicated because of side reactions on the aromatic substituent of bipyridine [23, 33]. Complex **Cu**•**6** was isolated by recrystallization of the precipitate obtained by the above process from an ethanol-methanol-water mixture (7:2:1). In addition, as a result of slow evaporation of the solution of this precipitate we were able to obtain the crystals of another minor form of copper complex **Cu**•**6**A, also suitable for X- ray. These newly obtained data suggest that the authors of [9] also synthesized mixtures of different forms of copper complexes, but only one of them was determined by X-ray in each case. Moreover, in addition to the X-ray data, only the results of elemental analysis are given in the article, and for each ligand they recorded a different form of the chelate.

The obtained chelates Cu•5 and Cu•6 were characterized by elemental analysis, IR, and mass spectra. In particular, in the IR spectra (Figures S11, S12), the vibrational bands of the carbonyl group in the region 1645-1674 cm⁻¹ can be observed. According to the previously described data [23, 34], the vibrational bands of the carbonyl group in the case of the corresponding 5-aryl-2,2'-bipyridin-6(6')-carboxylic acids are in the range of 1720-1744 cm⁻¹, i.e., one can conclude that the free ligands are absent from the composition of the obtained products. In addition, for Cu-6 complex it is important to note the absence of absorption bands of the cyano group in the region of 2220 cm⁻¹. The absorption spectra of the novel complexes in acetonitrile are also presented (Figure S13). In case of complex Cu-6A, the crystals were obtained in rather limited quantities, sufficient only for mass spectroscopy in addition to X-ray. In the absorption spectra two broad bands at 315 nm and 247-262 nm were discovered: the first one could be attributed to the $n \rightarrow \pi^*$ transitions, while the second one could be assigned to the $\pi \rightarrow \pi^*$ transitions (Figure S13).

According to X-ray data, the **Cu-6** complex is a dimer and crystallizes as a solvate with a methanol molecule. The geometry of a similar complex was shown earlier in [9], but the analysis of intermolecular interactions in the crystal was not presented by the authors. Each copper(II) atom in complex **Cu-6** has a distorted square planar coordination, where the Cu-Cu distance is 3.271 Å (Figure 1), whereas for the complex known in the literature it is 3.223 Å.

The hydrogen atom of the hydroxyl group of the solvated methanol molecule in the Cu•6 crystal forms a symmetric shortened O-H...O-type bifurcate contact with the participation of the oxygen atom of the carboxylate group of the ligand (the H...O distances are 2. 23(6) and 2.57(4) Å, O...O 3.03(1) and 3.15(5) Å, <OHO 163.4(5)° and 129.0(1)°)(Figure 2). In addition, the fluorine atom is involved in the formation of a weak intermolecular hydrogen bond with the hydrogen atom of the cyclopentane fragment (C-H...F 2.47(3) Å, C...F 3.24(9) Å. <CHF 136.7(5) °). Also, according to X-ray powder diffraction data, the homogeneity of this complex was confirmed (Figure S14). In case of Cu•6A, the structure was a binuclear complex in the form of a centrosymmetric dimer with bridging chlorides and a distorted square-pyramidal coordination of each copper ion (Figure 3).

In the structure of Cu-6A complex, copper(II) ions are coordinated by two nitrogen atoms and an oxygen atom of the tridentate ligand and two chlorine atoms. The plane of the square pyramidal Cu-centers consist of two nitrogen atoms and an oxygen atom of the chelate carboxylate ligand and one chlorine atom, while the apex is occupied by another chlorine atom, for which the Cu-Cl distance (Cu(1)-Cl(1) = 2.82(6) Å) is much longer than the Cu–Cl distance at the base of the pyramid (Cu(1)-Cl(1) = 2.23(1) Å). Thus, as a result of the coordination interaction of the Cu²⁺ ion with the ligand, two five-membered chelate rings CuC₂N₂ and CuC₂NO are enclosed. In this case, the Cu-N(1), Cu-N(2) and Cu-O(1) distances are equal to 1.93(8), 2.03(1) and 1.94(3) Å, respectively, and the N(1)-Cu(1)-N(2) and N(1)-Cu(1)-O(1) angles are 79.3(2)° and 81.4(0)°, respectively. It should be noted that this geometry is not specific to copper(II) complexes of the studied bipyridyl ligands [9, 11] and phenanthroline-substituted nitroxide radical [10].



Scheme 1 Reagents and conditions: *i*) pentafluorobenzene, *n*-BuLi, from -78 °C to o °C; *ii*) DDQ, EtOAc, reflux; *iii*) 2,5-norbornadiene/1,2-dichlorobenzene, reflux, 27 h; *iv*) NaOH / EtOH, rt, 12 h; v) CuCl₂•2H₂O / ethanol, 60 °C, 10 h.

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Scheme 2 Reagents and conditions: *i*) ethanol, 78 °C, 10 h.



2.23(6)Å

Figure 1 View of the structure of **Cu-6** depicted with 50% probability of displacement ellipsoids and showing the atomic labeling scheme (hydrogen atoms in organic ligands are not represented).

Figure 2 Participation of methanol solvate molecule in the formation of bifurcate intermolecular contact in the crystal of Cu+6.



Figure 3 View of the structure of **Cu+6A**, depicted with 50% probability of displacement ellipsoids (hydrogen atoms in organic ligands are not represented).

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Figure 4 Packing of molecules in complex Cu•6A, view along the a (a) and c (b) axes.

The supramolecular structure of the binuclear complex **Cu-6A** is shown in Figure 4. Herein, the crystal packing is formed mainly because of the interactions C(13)-H···O(1), C(9)-H···O(2) between the hydrogen atom of the fluorophenyl substituent or the hydrogen atom corresponding to one of the pyridyl rings and the oxygen atoms of the carboxylate (Table 1).

Besides, the packing of molecules into complex **Cu-6A** three-dimensional framework is created by hydrogen bond involving the hydrogen atom of the cyclopentane fragment and the fluorine atom $C(20)-H(20B)\cdots$ F with a distance of 2,45(4) Å. In this case, the lattice water molecule also could play an important role due to its tendency to be surrounded by the four nearest molecules of the binuclear complex and to form hydrogen bonds with them (see Table 1): its hydrogen atoms are oriented toward the O(1) and C(1) atoms, while its oxygen atom is oriented toward the hydrogen atom of one of the pyridyl rings.

Copper(II) complexes of 4-phenyl-1-(2-pyridyl)cyclopenteno[c]pyridine-3-carboxylate (CCDC 664383) and 5phenacyl-6-phenyl-3-(2-pyridyl)-1,2,4-triazine (CCDC 664386) were previously obtained and described [9]. In case of these complexes for the crystal packing of molecules, the following are essential hydrogen bonds of the type C_{Ph} -H...Cl or C-H...N, whereas in the case of complex **Cu·6A**, the crystal structure and packaging in the crystal are influenced by the crystallization water molecule and fluorine atoms.

The structure of **Cu•5** consists of discrete mononuclear units having copper, unlike complex **Cu•6A**, in a distorted octahedral coordination as shown in Figure 5.

In the case of the **Cu-5** complex, copper(II) is hexacoordinated and surrounded by four nitrogen atoms and two oxygen atoms of the tridentate ligands. Thus, copper(II) cation is located in the center of a distorted octahedron; three nitrogen atoms and an oxygen of the chelating carboxylate ligands occupy the corners of a distorted square base with the distances N(1)...N(2) 2.61(7) Å, N(2)...N(3) 3.51(5) Å, N(3)...O(1) 2.83(2) Å and O(1)...N(1) 2.58(5) Å. The remaining nitrogen atom and the oxygen atom of one of the ligands occupy the axial positions of the octahedron.

Table 1 Geometric parameters of hydrogen bonds in the crystal of**Cu•6A**.

D-HA	d(D-H), Å	d(D- HA), Å	<dha, th="" °<=""><th>d(DA), Å</th></dha,>	d(DA), Å
C(13)-HO(1)	0.93(1)	2.55(2)	163.3(2)	3.45(4)
C(9)-HO(2)	0.93(0)	2.59(5)	126.5(4)	3.23(6)
C(20)- H(20B)F(1)	0.97(0)	2.45(4)	117.8(7)	3.03(2)
O(3)- H(3B)O(1)	0.85(0)	2.14(7)	144.3(0)	2.88(1)
O(3)- H(3B)C(1)	0.85(0)	2.77(8)	150.8(0)	3.54(5)
C(10)- H(10)O(3)	0.93(1)	2.66(5)	116.9(0)	3.19(6)

* Hydrogen	bonds i	involvi	ng ator	ns of a	a solvate	e water m	olecul	e
are marked	with a	gray ba	ackgrou	ınd.				



Figure 5 View of the structure of **Cu-5** depicted with 50% probability of displacement ellipsoids and showing the atomic labeling scheme (hydrogen atoms are not represented).

The axial Cu–N (Cu(1)–N(4) = 2.41(2) Å) and Cu–O (Cu(1)–O(2) = 2.15(9) Å) distances are much longer than the equatorial ones (Cu(1)–N(1) = 1.93(4) Å; Cu(1)–N(2) = 2.26(2) Å; Cu(1)–N(3) = 1.96(8) Å; Cu(1)–O(1) = 2.03(8) Å), due to the Jahn–Teller effect, which was noted for transition metal compounds and for the most studied copper(II) compounds [35]. The lengths of the Cu–N bonds are consistent with the established patterns observed in structurally related copper(II) complexes that utilize bipyridyl ligands [11, 36].

N(1)-Cu(1)-The trans bond angles are $N(3) = 170.9(7)^{\circ}$, $O(1)-Cu(1)-N(2) = 157.8(2)^{\circ}$ and O(2)- $Cu(1)-N(4) = 153.3(4)^{\circ}$, deviating from the ideal value of 180°, indicating that the coordination geometry around copper is distorted octahedral. This distortion was shown to be typical of structurally related complexes of copper(II) with bipyridyl and phenanthroline ligands [36, 37], with the tetragonality parameter of 0.72 being calculated from the ratio of the average equatorial Cu-O/N bond lengths to the average axial Cu-O/N bond lengths (the average length of Cu-O/N equatorial bonds is 2.051 Å, while the average length of Cu-O/N axial bonds is 2.855 Å; their ratio is determined by the expression: 2.051 Å/2.855 Å = 0.72 [38]. Meanwhile, a complex system of intermolecular hydrogen bonds creates the main supramolecular motif of the organization of Cu-5 crystals in the form of parallel stacks formed along the *a* axis (Figure 6).

The oxygen atoms of the carboxyl group of one molecule of the **Cu**•**5** complex interact with two neighboring molecules *via* hydrogen bonds (Table 2), but one of these oxygen atoms formed a two-point heterosynthon C(26)-H...O(4), and the other ones forms a one-point heterosynthon C-H...O(1) (Figure 7).



Figure 6 Packing of **Cu**•**5** molecules in the form of a set of parallel stacks formed along the *a* axis.

Table 2 Geometric parameters of hydrogen bonds in a Cu•5 crystal.

D-HA	d(D-Н), Å	d(D- HA), Å	<dha, th="" °<=""><th>d(DA), Å</th></dha,>	d(DA), Å
C(26)- H(26)O(4)	0.93(0)	2.25(6)	155.2(0)	3.12(5)
C(8)- H(8)O(1)	0.93(0)	2.54(9)	156.2(4)	3.42(1)
C(5)- H(5)O(1)	0.93(0)	2.46(1)	136.9(9)	3.20(5)



Figure 7 View of various synthons surrounding the ${\bf Cu}{\boldsymbol{\cdot}}{\bf 5}$ complex molecule.

Besides, each of the perfluorophenyl substituents of the dipyridyl ligand participated in close intermolecular contacts with the adjacent aromatic ring, namely, the C...F interaction with a distance of 2.98(8) Å for the $C_6F_5...C_6F_5$ synthon and 3.091 Å for the $C_6F_5...C_6H_5$ synthon. There are some π – π overlap between the corresponding aromatic systems, but the distance between the centroids (Dcent 5.26(2) Å for the $C_6F_5...C_6H_5$ synthon) is too large to be energetically significant [39]. The structural role of intermolecular interactions in aromatic and fluoroaromatic molecules, such as the aryl-perfluoroaryl stacking synthon (Ar–ArF, C–H...F, C–F... π , and F...F interactions), was previously noted in a number of studies [40, 41].

4. Limitations

The developed approach is primarily limited by the number of metals that were used in the synthesis of metal complexes; when obtaining structures with other transition metals, one can expect the appearance of spatial features depending on the coordination number of the metal. Moreover, the utilization of different solvents, the ratio between salt and ligands, and temperature could affect the structure and other parameters of resulting complexes.

5. Conclusions

In summary, three novel Cu(II) complexes of (poly)fluorine-containing 5-aryl-2,2'-bipyridine-6(6')-carboxylic acids were obtained, the structures of which were studied by the XRD analysis. It was observed that the ligand containing one fluorine atom is prone to the formation of a coordination copper compound with the coordination number of five. On the other hand, it was found that in case of the ligand containing a polyfluoroaromatic fragment, the tridentate copper complex with the coordination number of six are formed. Supramolecular structure of the resulting chelates was hypothesized to be due to the influence of fluorine atoms involved in the formation of hydrogen bonds (in case of complexes Cu•6 and Cu•6A) or intermolecular short contacts of type C-F... π (in case of complex **Cu**•**5**), as well as the influence of the crystallization solvent molecules. The obtained data regarding the structure and properties of the developed coordination compounds could be used in the design of metal complexes and the study of the possibilities of their application as pharmacologically active compounds, chemosensors, and catalytic systems.

Abbreviation list

NMR – Nuclear Magnetic Resonance; TMS – Tetramethylsilane; CCDC – Cambridge Crystallographic Data Center; XRD – X-ray Diffraction; ESI-MS – Electrospray Ionisation Mass Spectrometry; DDQ – 2,3-dichloro-4,5-dicyanobenzoquinone.

Supplementary materials

This manuscript contains supplementary materials (NMR spectra), which are available on the corresponding online page.

Data availability statement

Data available within the article or its supplementary materials

Acknowledgments

This work was performed using the equipment of the Joint Use Center "Spectroscopy and Analysis of Organic Compounds" of the I. Ya. Postovsky Institute of Organic Synthesis of the Ural Branch of the Russian Academy of Sciences and also the equipment of the Center for Collective Use "Testing Center for Nanotechnology and Advanced Materials" of the Institute of Metal Physics of the Ural Branch of the Russian Academy of Sciences. Spectral data were obtained in the Laboratory of Complex Research and Expert Evaluation of Organic Materials, Center for Collective Use of unique equipment of the Ural Federal University, https://ckp.urfu.ru

Author contributions

Conceptualization: V.N.C., O.N.C Methodology: T.D.M., M.I.V., E.A.K., Y.B. Software: P.A.S. V.S.G., Y.B. Validation: D.S.K., G.V.Z. Formal analysis: D.S.K., G.V.Z. Investigation: A.P.K., M.I.V., E.A.K., Y.M.S, Data Curation: A.V.R., P.A.S., V.S.G. Visualization: A.V.R. Supervision: M.V.V., V.N.C., O.N.C. Writing – original draft: T.D.M, D.S.K. Writing – review & editing: M.V.V, T.D.M, D.S.K. Project administration: M.V.V.

Conflict of interest

The authors declare no conflict of interest

Additional information

Author IDs:

Timofey D. Moseev, Scopus ID <u>57196048249</u>; Mikhail V. Varaksin, Scopus ID <u>26637829900</u>; Alexey P. Krinochkin, Scopus ID <u>56951324100</u>; Maria I. Valieva, Scopus ID <u>57204922642</u>; Ekaterina A. Kudryashova, Scopus ID <u>57359251800</u>; Yulia M. Sayfutdinova, Scopus ID <u>59308210300</u>; Anastasiya V. Rybakova, Scopus ID <u>57204912787</u>; Dmitry S. Kopchuk, Scopus ID <u>14123383900</u>; Grigory V. Zyryanov, Scopus ID <u>6701496404</u>; Pavel A. Slepukhin, Scopus ID <u>6506482417</u>; Vasiliy S. Gaviko, Scopus ID <u>7006478992</u>; Valery N. Charushin, Scopus ID <u>7006350819</u>; Oleg N. Chupakhin, Scopus ID <u>7006259116</u>.

Websites:

Ural Federal University, <u>https://urfu.ru/en/;</u> Institute of Organic Synthesis, UB RAS, <u>https://iosuran.ru/;</u> South Ural State University, <u>https://www.susu.ru/en;</u> Institute of Physics of Metals, UB RAS, <u>https://www.imp.uran.ru/?q=en/</u>.

References

- Golubeva YA, Lider EV. Copper(ii) complexes based on 2,2'bipyridine and 1,10-phenanthroline as potential objects for developing antitumor drugs. J Struct Chem. 2024;65(6):1159– 1209. doi:10.1134/s0022476624060088
- Dorairaj DP, Kumar P, Rajasekaran H, Bhuvanesh N, Hsu SCN, Karvembu R. Copper(II) complexes containing hydrazone and bipyridine/phenanthroline ligands for anticancer application against breast cancer cells. J Inorg Biochem. 2025;262(112759):112759. doi:10.1016/j.jinorgbio.2024.112759
- Shchegolkov EV, Shchur IV, Burgart YV, Slepukhin PA, Evstigneeva NP, Gerasimova NA, Zilberberg NV, Kungurov NV, Saloutin VI, Chupakhin ON. Copper(II) and cobalt(II) complexes based on methyl trifluorosalicylate and bipyridine-type ligands: Synthesis and their antimicrobial activity. Polyhedron. 2021;194(114900):114900. doi:10.1016/j.poly.2020.114900
- Korpi H, Sippola V, Filpponen I, Sipilä J, Krause O, Leskelä M, Repo T. Copper-2,2'-bipyridines: Catalytic performance and structures in aqueous alkaline solutions. Appl Catal A Gen. 2006;302(2):250–256. doi:10.1016/j.apcata.2006.01.020
- 5. Romo AIB, dos Reis MP, Nascimento OR, Bernhardt PV, Rodríguez-López J, Diógenes ICN. Interplay of electronic and geometric structure on Cu phenanthroline, bipyridine and derivative complexes, synthesis, characterization, and reactivity towards oxygen. Coord Chem Rev.
- 2023;477(214943):214943. doi:10.1016/j.ccr.2022.214943
 Burgart Y, Shchegolkov E, Shchur I, Kopchuk D, Gerasimova N, Borisevich S, Evstigneeva N, Zyryanov G, Savchuk M, Ulitko M, Zilberberg N, Kungurov N, Saloutin V, Charushin V, Chupakhin O. Promising antifungal and antibacterial agents based on 5-aryl-2.2'-bipyridines and their heteroligand salic-
- based on 5-aryl-2,2'-bipyridines and their heteroligand salicylate metal complexes: Synthesis, bioevaluation, molecular docking. ChemMedChem. 2022;17(3):e202100577 doi:10.1002/cmdc.202100577
- Safin DA, Mitoraj MP, Robeyns K, Filinchuk Y, Vande Velde CML. Luminescent mononuclear mixed ligand complexes of copper(i) with 5-phenyl-2,2'-bipyridine and triphenylphosphine. Dalton Trans. 2015;44(38):16824–16832. doi:10.1039/c5dt02755a
- Tong J, Zhao L-R, Zhang J, Wang X-Y, Yu Y-M, Yu S-Y. Heteroleptic copper(i) complexes bearing functionalized 1*H*-pyrazole-bipyridine ligands: synthesis, photophysical properties, crystal structures, and applications in halogen sensing. New J Chem. 2023;47(9):4374–4385. doi:10.1039/d2nj05408f

- Prokhorov AM, Slepukhin PA, Kozhevnikov DN. CuCl₂ induced reactions of 6-ethynyl- and 6-cyano-5-aryl-2,2'-bipyridines with various N- and O-nucleophiles in comparison with the reactions of relative 1,2,4-triazines. J Organomet Chem. 2008;693(10):1886-1894. doi:10.1016/j.jorganchem.2008.02.016
- Gao D-Z, Sun Y-Q, Liao D-Z, Jiang Z-H, Yan S-P. Synthesis and crystal structures of two metal-nitroxide complexes including a phenanthroline-substituted nitroxide radical. J Coord Chem. 2008;61(15):2413-2421. doi:10.1080/00958970801914082
- 11. Maheswari PU, Lappalainen K, Sfregola M, Barends S, Gamez P, Turpeinen U, Mutikainen I, van Wezel GP, Reedijk J. Structure and DNA cleavage properties of two copper(ii) complexes of the pyridine-pyrazole-containing ligands mbpzbpy and Hmpzbpya. Dalton Trans. 2007;33:3676. doi:10.1039/b704390b
- Moghimi A, Alizadeh R, Aghabozorg H, Shockravi A, Aragoni MC, Demartin F, Isaia F, Lippolis V, Harrison A, Shokrollahi A, Shamsipur M. Ion pairing, H-bonding, and π-π interactions in copper(II) complex-organo-networks derived from a proton-transfer compound of the 1,10-phenanthroline-2,9-dicarboxylic acid. J Mol Struct. 2005;750(1-3):166–173. doi:10.1016/j.molstruc.2005.04.031
- Stipurin S, Strassner T. C^C* platinum(II) complexes with electron-withdrawing groups and beneficial auxiliary ligands: Efficient blue phosphorescent emission. Inorg Chem. 2021;60(15):11200-11205. doi:10.1021/acs.inorgchem.1c01172
- Khavasi HR, Rahimi N. Fluorine-substituted ligands induce structural diversity of coordination compounds. ChemistrySelect. 2017;2(34):11314–11321. doi:10.1002/slct.201702047
- Honzíčková I, Vinklárek J, Romão CC, Růžičková Z, Honzíček J. Novel indenyl ligands bearing electron-withdrawing functional groups. New J Chem. 2016;40(1):245–256. doi:10.1039/c5nj02406d
- Berger R, Resnati G, Metrangolo P, Weber E, Hulliger J. Organic fluorine compounds: a great opportunity for enhanced materials properties. Chem Soc Rev. 2011;40(7):3496. doi:10.1039/cocs00221f
- Páez-Franco JC, Zermeño-Ortega MR, de la O-Contreras CM, Canseco-González D, Parra-Unda JR, Avila-Sorrosa A, Enríquez RG, Germán-Acacio JM, Morales-Morales D. Relevance of fluorinated ligands to the design of metallodrugs for their potential use in cancer treatment. Pharmaceutics. 2022;14(2):402. doi:10.3390/pharmaceutics14020402
- 18. CrysAlisPro, version 1.171.39.38a, Data Collection, Reduction and Correction Program, Rigaku Oxford Diffraction, 2017.
- Sheldrick GM. SHELXT- Integrated space-group and crystalstructure determination. Acta Crystallogr A Found Adv. 2015;71(1):3-8. doi:10.1107/s2053273314026370
- 20. Sheldrick GM. Crystal structure refinement with *SHELXL*. Acta Crystallogr C Struct Chem. 2015;71(1):3–8. doi:10.1107/s2053229614024218
- 21. Dolomanov OV, Bourhis LJ, Gildea RJ, Howard JAK, Puschmann H. *OLEX2*: a complete structure solution, refinement and analysis program. J Appl Crystallogr. 2009;42(2):339– 341. doi:10.1107/s0021889808042726
- Shabunina OV, Starnovskaya ES, Shtaits YK, Kopchuk DS, Kovalev IS, Zyryanov GV, Rusinov VL, Chupakhin ON. A Modified Synthesis of 6-Aryl-3-(6-R-pyridin-2-yl)-1,2,4-triazines. Russ J Org Chem. 2018;54(10):1576–1578. doi:10.1134/s107042801810024x
- Krinochkin AP, Kopchuk DS, Kozhevnikov DN. Luminescent neutral lanthanide complexes of 5-aryl-2,2'-bipyridine-6-carboxylic acids, synthesis and properties. Polyhedron. 2015;102:556–561. doi:10.1016/j.poly.2015.09.055
- 24. Moseev TD, Varaksin MV, Gorlov DA, Nikiforov EA, Kopchuk DS, Starnovskaya ES, Khasanov AF, Zyryanov GV, Charushin VN, Chupakhin ON. Direct C H/C Li coupling of 1,2,4-triazines with C_6F_5Li followed by aza-Diels-Alder reaction as a pot, atom, and step economy (PASE) approach towards novel

fluorinated 2,2'-bipyridine fluorophores. J Fluor Chem. 2019;224:89–99. doi:10.1016/j.jfluchem.2019.05.008

- Prokhorov AM., Kozhevnikov DN. 2012. Reactions of triazines and tetrazines with dienophiles (Review). Chem Heterocycl Comp. 2012;48(8):1153–1176. doi:10.1007/s10593-012-1117-9
- Zhang F-G, Chen Z, Tang X, Ma J-A. Triazines: Syntheses and Inverse Electron-demand Diels-Alder Reactions. Chem Rev. 2021;121(23):14555-14593. doi:10.1021/acs.chemrev.1coo611
- Chupakhin ON, Postovskii IYa. Nucleophilic Substitution of Hydrogen in Aromatic Systems. Russ Chem Rev. 1976;45(5):454-468. doi:<u>RC1976v045n05ABEH002670</u>
- Charushin VN, Chupakhin ON. 2014. Metal Free C-H Functionalization of Aromatics, Nucleophilic Displacement of Hydrogen, in Topics in Heterocyclic Chemistry, eds. V. Charushin and O. Chupakhin, Springer. 2014;37:1-50.
- 29. Kovalev IS, Kopchuk DS, Zyryanov GV, Rusinov VL, Chupakhin ON, Charushin VN. Organolithium compounds in the nucleophilic substitution of hydrogen in arenes and hetarenes. Russ. Chem. Rev. 2015;84(12):1191-1225. doi:10.1070/RCR4462
- 30. Fatykhov RF, Savchuk MI, Starnovskaya ES, Bobkina MV, Kopchuk DS, Nosova EV, Zyryanov GV, Khalymbadzha IA, Chupakhin ON, Charushin VN, Kartsev VG. Nucleophilic substitution of hydrogen-the Boger reaction sequence as an approach towards 8-(pyridin-2-yl)coumarins. Mendeleev Commun. 2019;29(3):299-300. doi:10.1016/j.mencom.2019.05.019
- Konno S, Sagi M, Takaharu E, Fujimura S, Hayashi K, Yamanaka H. Studies on as-Triazine Derivatives. XII.: Synthesis of Alkenyl-1,2,4-triazine Derivatives. Chem. Pharm. Bull. 1988;36(5):1721-1726. doi:10.1248/cpb.36.1721
- Kozhevnikov DN, Kozhevnikov VN, Prokhorov AM, Ustinova MM, Rusinov VL, Chupakhin ON,Aleksandrov GG, König B. Consecutive nucleophilic substitution and aza Diels-Alder reaction—an efficient strategy to functionalized 2,2'-bipyridines. Tetrahedron Lett. 2006;47(6):869-872. doi:10.1016/j.tetlet.2005.12.006
- 33. Slovesnova NV, Minin AS, Belousova AV, Ustyugov AS, Chaprov KD, Krinochkin AP, Valieva MI, Shtaitz YaK, Starnovskaya ES, Nikonov IL, Tsmokalyuk AN, Kim GA, Santra S, Kopchuk DS, Nosova EV, Zyryanov GV. New TEMPO-Appended 2,2'-Bipyridine-Based Eu(III), Tb(III), Gd(III) and Sm(III) Complexes: Synthesis, Photophysical Studies and Testing Photoluminescence-Based Bioimaging Abilities. Molecules. 2022;27(23):8414. doi:10.3390/molecules27238414
- Kopchuk DS, Krinochkin AP, Kozhevnikov DN, Slepukhin PA. Novel neutral lanthanide complexes of 5-aryl-2,2'-bipyridine-6'-carboxylic acids with improved photophysical properties. Polyhedron. 2016;118:30–36. doi:10.1016/j.poly.2016.07.025
- Halcrow MA. Jahn–Teller distortions in transition metal compounds, and their importance in functional molecular and inorganic materials. Chem Soc Rev. 2013;42(4):1784–1795. doi:10.1039/c2cs35253b
- 36. Sharma Mitu, Ganeshpandian M, Majumder M, Tamilarasan A, Sharma Mukesh, Mukhopadhyay R, Islam NS, Palaniandavar M. Octahedral copper(ii)-diimine complexes of triethylenetetramine: effect of stereochemical fluxionality and ligand hydrophobicity on Cu^{II}/Cu^Iredox, DNA binding and cleavage, cytotoxicity and apoptosis-inducing ability. Dalton Trans. 2020;49(24):8282–8297. doi:10.1039/dodto0928h
- Iqbal M, Ali S, Tahir MN. Octahedral copper(II) carboxylate complex: synthesis, structural description, DNA-binding and anti-bacterial studies. J Coord Chem. 2018;71(7):991–1002. doi:10.1080/00958972.2018.1456655
- Matović ZD, Miletić VD, Ćendić M, Meetsma A, van Koningsbruggen PJ, Deeth RJ. Synthetic, crystallographic, and computational study of copper(II) complexes of ethylenediaminetetracarboxylate ligands. Inorg Chem. 2013;52(3):1238– 1247. doi:10.1021/ic301609t
- 39. Vangala VR, Nangia A, Lynch VM. Interplay of phenyl-perfluorophenyl stacking, C-H…F, C-F… π and F…F interactions in some crystalline aromatic azinesElectronic supplementary

information (ESI) available: experimental powder X-ray diffraction spectra. See http://www.rsc.org/suppdata/cc/b2/b202181a/.Chem Com-

mun (Camb). 2002;12:1304-1305. doi:10.1039/b202181a

- 40. Bonegardt DV, Trubin SV, Sukhikh AS, Klyamer DD, Basova TV. Effect of substituent position on saturated vapor pressure of tetrafluorosubstituted zinc phthalocyanines. Žurnal neorganičeskoj himii. 2023;68(2):181–190. doi:10.31857/s0044457x22601614
- 41. CAdams N, Cowley AR, Dubberley SR, Sealey AJ, Skinner MEG, Mountford PEvaluation of the relative importance of Ti-l···H-N hydrogen bonds and supramolecular interactions be-tween perfluorophenyl rings in the crystal structures of [Ti(NR)Cl₂(NHMe₂)₂] (R = iPr, C₆H₅ or C₆F₅)Electronic supplementary information (ESI) available: characterisation and crystal data for compounds 1–3. See http://www.rsc.org/suppdata/cc/b1/b109251k/. Chem Com-

mun (Camb). 2001;24:2738–2739. doi:10.1039/b109251k/