Journal of the Serbian Chemical Society
JSCS@tmf.bg.ac.rs • www.shd.org.rs/JSCS
J. Serb. Chem. Soc. *86* (10) 901–915 (2021)
JSCS–5471
Original scientific paper
Published 9 September 2021

Synthesis and properties of new fused pyrrolo-1,10-phenanthroline type derivatives

CRISTINA M. AL-MATARNEH[1,2]*, IRINA ROSCA[1], SERGIU SHOVA[1] and RAMONA DANAC[2]**

[1]*"Petru Poni" Institute of Macromolecular Chemistry of Romanian Academy, 41A Grigore Ghica Voda Alley, Iasi 700487, Romania and* [2]*Chemistry Department, Faculty of Chemistry, "Al. I. Cuza" University of Iasi, 11 Carol I, Iasi 700506, Romania*

(Received 19 August 2020, revised 10 July, accepted 13 July 2021)

Abstract: New fused pyrrolo-phenanthroline type derivatives were synthesized, in two steps, from 1,10-phenanthroline and evaluated for antimicrobial activity and fluorescence properties. Our synthetic approach involved a 3+2 dipolar-cycloaddition of some selected *N*-substituted 1,10-phenanthrolin-1-ium ylides, (m)ethoxycarbonyl and cyano (1,2-di)substituted acetylenes and alkenes, respectively. The structures of compounds were supported by analytical and spectroscopic data. The molecular structures of four selected compounds have also been also determined by monocrystal XRD analyses. All synthesized compounds were then evaluated for their potential antimicrobial activity against *Staphylococcus aureus* ATCC25923, *Escherichia coli* ATCC25922 and *Candida albicans* ATCC10231. Two of the compounds demonstrated significant activity against the above tested strains.

Keywords: azahetarenes; 1,3-dipolar-cycloaddition; antimicrobial activity; fluorescence; phenanthrolinium-*N*-ylides.

INTRODUCTION

1,10-Phenanthroline is, "traditionally", a privileged moiety, being endowed with a series of significant properties such as the convenient placement of the nitrogen atoms which make it a valuable chelating bidentate ligand used for the detection or removal of metal ions, and the rigid planar structure with an extended π-conjugation, thus conferring challenging semiconducting and emissive properties. Moreover, due its specific structure, 1,10-phenanthroline has a good intercalation ability with DNA base pairs, being an excellent scaffold of choice in the generation of unique bioactive compounds.[1–3]

*,** Corresponding authors. E-mail: (*)almatarneh.cristina@icmpp.ro; (**)rdanac@uaic.ro
https://doi.org/10.2298/JSC200819057A

1,10-Phenanthroline derivatives have found various uses in domains like solid-state device technology, particularly organic light emitting diodes (OLEDs),[4,5] luminescence[6] or pharmacology.[7–10]

However, the main drawback of using 1,10-phenanthroline derivatives as drugs consists of their toxicity given by its intrinsic chelating nitrogen atoms that can inhibit diverse metalloenzymes.[8] Therefore, an adopted strategy for the reduction of the toxicity, without affecting the planar geometry of 1,10-phenanthroline mandatory for the DNA intercalation, is the "locking" of one of the nitrogen atoms. This can involve, for example, the quaternization of one of the nitrogen atoms by forming monoquaternary salts,[7,8] or the synthesis of fused 1,10-phenanthroline compounds in which just one nitrogen atom is bridgehead.[7]

On the other hand, the fusion of two or more heterocyclic rings is a well-known strategy leading to new classes of condensed heterosystems, many of them providing different properties against to the initial ones.

On the other hand, pyrrole is equally an important nitrogen containing heterocycle, largely documented in pharmaceuticals, agrochemicals, solar batteries, OLED's and organic semiconductors chemistry.[11–13]

Fluorine incorporation into biologically active molecules confers modifications in their chemical, physical, and biological properties. From the medicinal point of view, this is an important motif because of its stereoelectronic properties.[14] The trifluoromethyl group can increase lipophilicity of a molecule to improve its *in vivo* transport. Also, the formation of secondary metabolites is reduced because of the strength of the C-F bond.[15]

Using some structural combination strategies, several series of fused pyrrolophenanthroline derivatives were so far reported to possess not only bio-impact, but also other interesting properties, in order to increase the structural diversity of the potential biological active compounds.[16-18]

From the synthetic point of view, the methods for obtaining pyrrolo[1,2-*a*]-[1,10]phenanthrolines are very limited. 1,3-Dipolar cycloaddition reactions of phenanthrolinium *N*-ylides to π-deficient alkynes or alkenes is one of the most useful strategies to afford pyrrolo-phenanthroline derivatives.[19–22] Multicomponent condensation reactions,[23-24] different cyclization reactions including domino-Knoevenagel-cyclization,[22,25] or one pot four component microwave-assisted reactions[18,26] are the additional reported pathways to form pyrrolo[1,2-*a*]-[1,10]phenanthroline fused system.

As a continuation of our research focused on phenanthrolines fused systems[27–30] and as part of our concern in the field of biologically active compounds,[31–35] the purpose of our present study was to synthesize new 1,10-phenanthroline derivatives having one of its *N*-atoms locked in order to ensure a potential bio-activity (by maintaining the rings coplanarity and reducing the toxicity due to *N*-atoms internal chelating propensity). Thus, herein we report the syn-

thesis, structure, fluorescence and the *in vitro* antimicrobial evaluation of several new 1,10-phenanthroline derivatives.

EXPERIMENTAL

Chemistry

Melting points were recorded on an A. Krüss Optronic melting point meter KSPI and are uncorrected. 1D-, 2D-, ^{1}H- and ^{13}C-NMR spectra were recorded on a Bruker Avance III 500 instrument operating at 500 or 125 MHz for ^{1}H- and ^{13}C nuclei, respectively. All chemical shifts (δ values) are given in parts per million (ppm); all homo- and heterocoupling patterns (^{n}J values) are given in Hertz (Hz). No TMS was added, chemical shifts were measured against the solvent peak. IR spectra were recorded on a FTIR Shimadzu or Jasco 660 plus FTIR spectrophotometer. Thin layer chromatography (TLC) was carried out on Merck silica gel 60F_{254} plates. Visualization of the plates was achieved using a UV lamp (λ_{max} = 254 or 365 nm). UV–Vis spectra were recorded on a Lambda 35, Perkin Elmer spectrometer. Fluorescence measurements were carried out using a Fluoromax 4, Horiba fluorescence spectrophotometer. All commercially available products were used without further purification unless otherwise specified.

*General procedure for synthesis of salts **3***

To an acetone (5mL) solution containing 1,10-phenanthroline (1 mmol), the corresponding 4-(tri)fluoro(methyl)phenacyl bromide (1.1 mmol) was added. The reaction mixture was stirred at room temperature over the night. After this period, the resulted suspension was filtered off and the solid was washed with acetone to give the desired product.

The following compounds were synthesized:

- 1-[2-(4-Fluorophenyl)-2-oxoethyl]-1,10-phenanthrolin-1-ium bromide (**3a**);
- 1-[2-(4-Trifluoromethylphenyl)-2-oxoethyl]-1,10-phenanthrolin-1-ium bromide (**3b**).

*General procedure for synthesis of compounds **4**–**7***

At room temperature and under inert atmosphere, to a dichloromethane (5 mL) suspension containing the cycloimmonium salt (1 mmol) and dipolarophile (dimethylacetylene dicarboxylate (DMAD), ethyl propiolate (EP), acrylonitrile or fumarodinitrile, 1.1 mmol) triethylamine (TEA, 3 mmol) was added dropwise over 1 h with vigorous stirring. The reaction mixture was then stirred over the night at room temperature (rt). Methanol (5 mL) was added and the resulting mixture was kept over the night without stirring. The resulted suspension was filtered off to give a solid that was washed with methanol. The crude product was then crystallized from an appropriate solvent (reported in Supplementary material to this paper for each compound).

The following compounds were synthesized:

- Dimethyl 11-(4-fluorobenzoyl)-10,11-dihydropyrrolo[1,2-*a*][1,10]phenanthroline-9,10--dicarboxylate (**4a**);
- Dimethyl 11-[4-(trifluoromethyl)benzoyl]-10,11-dihydropyrrolo[1,2-*a*][1,10]phenanthroline-9,10-dicarboxylate (**4b**);
- Ethyl 11-(4-fluorobenzoyl) pyrrolo[1,2-a][1,10]phenanthroline-9-carboxylate (**5a**);
- Ethyl 11-[4-(trifluoromethyl)benzoyl]pyrrolo[1,2-a][1,10]phenanthroline-9-carboxylate (**5b**);
- 11-(4-Fluorobenzoyl)-10,11-dihydropyrrolo[1,2-a][1,10]phenanthroline-9-carbonitrile (**6a**);
- 11-[4-(Trifluoromethyl)benzoyl]-10,11-dihydropyrrolo[1,2-a][1,10]phenanthroline-9--carbonitrile (**6b**);

• 11-(4-Fluorobenzoyl)-8a,9-dihydropyrrolo[1,2-a][1,10]phenanthroline-9,10-dicarbonitrile (**7a**);

• 11-[4-(Trifluoromethyl)benzoyl]-8a,9,10,11-tetrahydropyrrolo[1,2-a][1,10]phenanthroline-9-carbonitrile (**7b**).

The physical and spectral data for compounds **3**–**7** are provided in the Supplementary material of this paper.

X-Ray crystallography

X-ray diffraction measurements were carried out with a Rigaku Oxford-Diffraction Xcalibur E CCD diffractometer equipped with graphite-monochromated MoKα radiation. Single crystals were positioned at 40 mm from the detector and 325 frames were measured each for 30 s over 1° scan width. The unit cell determination and data integration were carried out using the CrysAlis package of Oxford Diffraction.[36] The structures were solved by Intrinsic Phasing using Olex2[37] software with the SHELXT[38] structure solution program and refined by the full-matrix least-squares on F^2 with SHELXL-2015[39] using an anisotropic model for non-hydrogen atoms. All H atoms were introduced in idealized positions (d_{CH} = 0.96 Å) using the riding model with their isotropic displacement parameters fixed at 120 % of their riding atom. The molecular plots were obtained using the Olex2 program. The crystallographic data and the refinement details are given in Table S-I (Supplementary material to this paper) as CCDC 2056678 (for **4b**), 2015662 (for **6a**), 2056679 (for **6b**) and 2056680 (for **7b**). These data can be obtained free of charge from the Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif.

Photophysical investigations (UV–Vis and fluorescence spectra)

Spectroscopic grade solvents were used for the photophysical characterization of the synthesized derivatives. UV–Vis measurements were performed on a Lambda 35 device (Perkin Elmer, USA). The absorption spectra were measured in the 270–700 nm range for identical sample volumes (3 mL) with the following parameters: slit width 1 nm, scan speed 480 nm/ /min and data interval 1 nm. The spectra of the samples were measured at room temperature using 1 cm path length quartz cuvettes. The UV–Vis absorption and the emission spectra of 1,10-phenanthroline derivatives employed in this study were recorded in dilute solution (2×10^{-7} mol/L) using dimethylsulfoxide (DMSO). Fluorescence measurements were carried out using a FluoroMax-4 spectrophotometer (Horiba, Kyoto, Japan). The emission spectra were collected using an excitation wavelength of 292 nm.

Antimicrobial activity

The antimicrobial activity was determined by disk diffusion assay against three different reference strains: *Staphylococcus aureus* ATCC25923, *Escherichia coli* ATCC25922 and *Candida albicans* ATCC10231. All microorganisms were stored at –80 °C in 20 % glycerol. The bacterial strains (*S. aureus* and *E. coli*) were refreshed in Mueller-Hinton broth at 36±1 °C, and the yeast strain (*C. albicans*) was refreshed on Sabouraud dextrose broth at 36±1 °C. Microbial suspensions were prepared with these cultures in sterile solution in order to obtain the turbidity optically comparable to that of 0.5 McFarland standards (yielding a suspension containing 10^8 CFU mL^{-1} for all the microorganisms).

Volumes of 0.4 mL from each inoculum were spread onto Mueller–Hinton agar and Sabouraud dextrose agar and all the tested samples were added after the medium surface dried. The sterilized paper discs (6 mm) were placed on the plate and an aliquot (20 μL) of the tested compounds (concentration 100 mg/mL, dissolved in DMSO) was added on the paper discs. As controls it was used Trimethoprim 98 % (TMP, Acros Organics, New Jersey, USA)

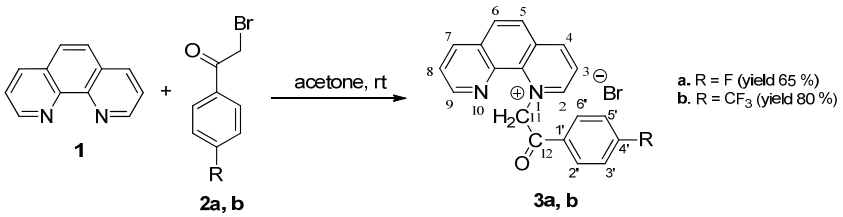
against the bacterial strains and nystatin 85+ % (NS) (Acros Organics, New Jersey, USA) against the yeast strain at the same concentrations as the tested compounds. To evaluate the antimicrobial properties, the growth inhibition was measured under standard conditions after 24 h of incubation at 36±1 °C. After the incubation, the diameters of inhibition zones were measured by using Image-J software. Minimum inhibitory concentration (*MIC*) was determined from a 10-dilution series starting from 100 mg/mL.

RESULTS AND DISCUSSION

Synthesis and characterization

Our strategy to access the pyrrolo[1,2-*a*][1,10]phenanthroline skeleton involved a two steps sequence including first the monoquaternization of 1,10-phenanthroline, and second, the 3+2 dipolar-cycloaddition of the azomethine ylides, generated *in situ* from the monoquaternary salts, to different dipolarophiles.

Thus, monoquaternary salts **3a** and **b** were obtained with excellent yields by an *N*-alkylation reaction of 1,10-phenanthroline **1** with 2-bromo-4'-fluoroacetophenone **2a** or 2-bromo-4'-trifluoromethylacetophenone **2b** (Scheme 1). Compound **3a** was previously reported, the analytical data being in accordance to the literature.[40]



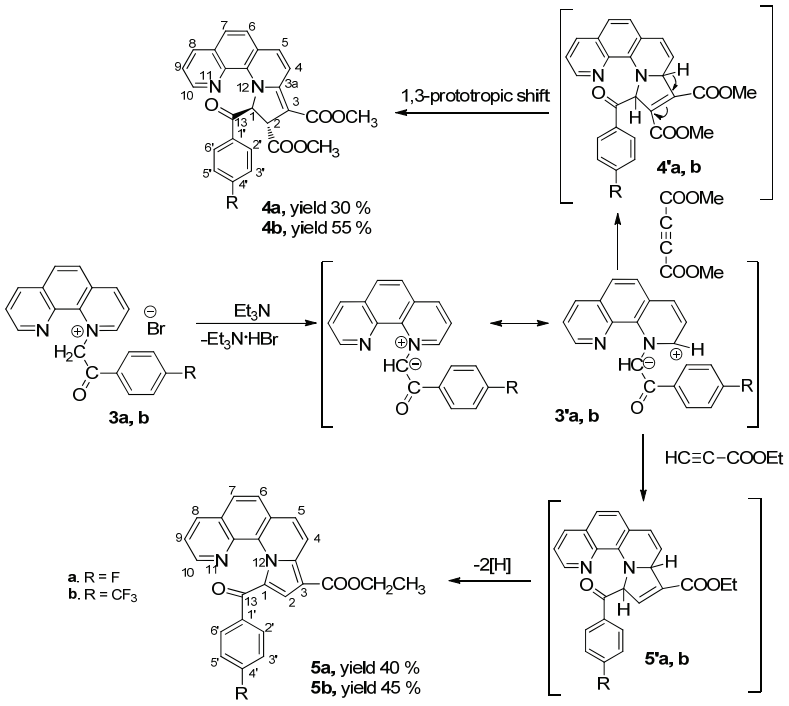
1 **2a, b** **3a, b**

Scheme 1. Synthesis of monoquaternary salts **3a** and **b**.

Next step was the dipolar cycloaddition of the ylides **4'a** and **b** (generated *in situ* upon triethylamine treatment from the corresponding salts **3a** and **b**) to dimethylacetylene dicarboxylate (DMAD) and ethyl propiolate (EP), respectively (Scheme 2).

An earlier insight concerning the cycloadditions of the *N*-ylide **3'a** to DMAD and EP was previously reported by Dumitrascu *et al*., using similar reaction conditions.[41] While, from the reaction of **3'a** with EP, only one single regioisomer of the expected aromatic pyrrolo[1,2-*a*][1,10]phenanthroline **5a** has been isolated in accordance with the reported data,[41] the reaction of **3'a** with DMAD, led, to the new 10,11-dihydropyrrolo[1,2-*a*][1,10]phenanthroline derivative **4a** (Scheme 2) in a moderate yield. The compound **4a** was different with respect to the those reported in Ref 41 (a mixture of similar substituted 8*a*,9-dihydropyrrolo[1,2-*a*][1,10]phenanthroline and pyrrolo[1,2-*a*][1,10]phenan-throline derivatives) by the position of the double bond in the pyrrole ring. Thus, our NMR data of compound **4a** clearly revealed that the double bond was, in fact,

located between C-3 and C-3a atoms of the fused pyrrole ring. Similarly, the compounds **4b** and **5b** were also obtained in the reaction between *N*-ylide **3'b** with DMAD and EP, respectively.



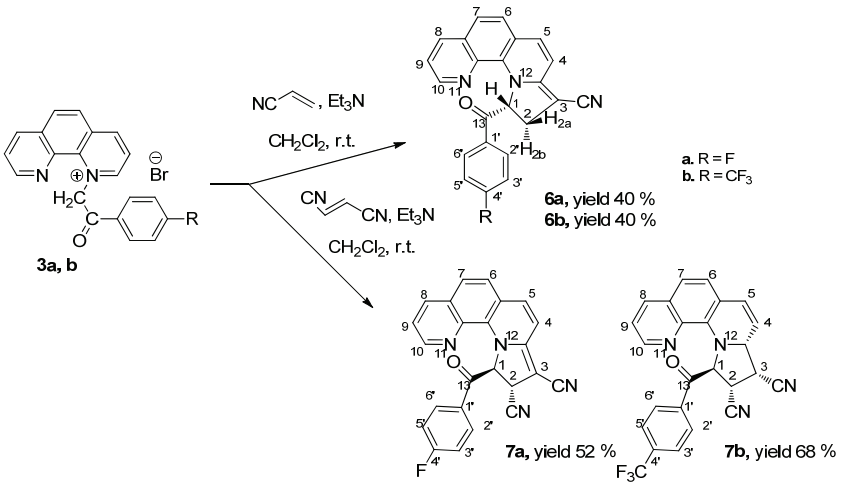
Scheme 2. Proposed reaction pathways for the synthesis of compounds **4a** and **b** and **5a** and **b**.

Thus, it was assumed that the cycloaddition resulted initially in the formation of no isolable 8*a*,11-dihydropyrrolo[1,2-*a*][1,10]phenanthroline intermediates **4'a** and **b** and **5'a** and **b**, respectively, which next underwent different pathways: an oxidative aromatization in case of **5'a** and **b** (converting them into the more stable aromatic compounds, **5a** and **b**) and a 1,3-protopropic shift (initiated by the excess of TEA) in the case of **4'a** and **b** leading to the compounds **4a** and **b** (Scheme 2).

By comparing the magnitude of the coupling pattern $^{3}J_{H,H}$(H-1/H-2), exhibited by compound **4a** (5.0 Hz), with the ones reported for other similar compounds (4.8 Hz), whose X-ray molecular structure displayed the geometry of the dihydropyrrole ring,[40] it was clear that substituents at C-1 and C-2 were located in a *trans*-configuration, *i.e.*, 1S*, 2S*. Next, spectral data (IR, NMR) of compound **5a** were in accordance with those reported in the literature.[40]

Next, the similar conditions were created (dichloromethane as solvent at room temperature) for the cycloaddition of the *N*-ylide **3'a** and **b** to acrylonitrile

and fumarodinitrile, respectively (Scheme 3). Each reaction afforded just a single regioisomeric (**3a** and **b** → **6a** and **b**) or diastereomeric (**3a** → **6a**, but **3b** → **7b**) product. Thus, in the case of salt **3a**, the both compounds obtained **6a** and **7a** proved to possess a 10,11-dihydropyrrolo[1,2-*a*][1,10]phenanthroline structure (Scheme 3). In the case of salt **3b** (issued from the reaction with fumarodinitrile), the compound **6b** with 8a,9,10,11-tetrahydropyrrolo[1,2-*a*][1,10]phenanthroline structure was produced, while in the case of reaction with acrylonitrile, the compound **7b** with 10,11-dihydropyrrolo[1,2-*a*][1,10]phenanthroline structure was isolated (Scheme 3). Compounds **6a** and **b** and **7a** were formed during the subsequent partial oxidation of a tetrahydropyrrolo[1,2-*a*][1,10] phenanthroline type intermediates, which is supposed to be formed in the first stage.[20]



Scheme 3. Synthesis of compounds **6a** and **b** and **7a** and **b**.

As for compound **4a** and also in the case of compound **7a**, we re-found the same size of the coupling pattern, namely $^{3}J_{H,H}$(H-1/H-2) = 5.0 Hz, that we assigned, once again, to a *trans*-arrangement (1S*, 2S*) of the ligands –CN and 4-fluorobenzoyl.

All (poly)chiral compounds **4a, b**, **7a** and **7b** were obtained as major racemates.

The results of X-ray diffraction study for compounds **4b**, **6a**, **6b** and **7b** are shown in Fig. 1. The selected bond distances and angles are summarized in Table S-I of trhe Supplementary material. According to X-ray crystallography, all the compounds crystallized with one molecule in the asymmetric part. There is no co-crystallized solvent molecule in all the crystals. As it was expected, due to steric hindrance, all the molecules exhibit essentially non-planar conformation. The dihedral angle between two sets of co-planar atoms were found to be of 74.83(8), 87.88(16), 99.1(3) and 110.2(1) for **4b**, **6a**, **6b** and **7b**, respectively.

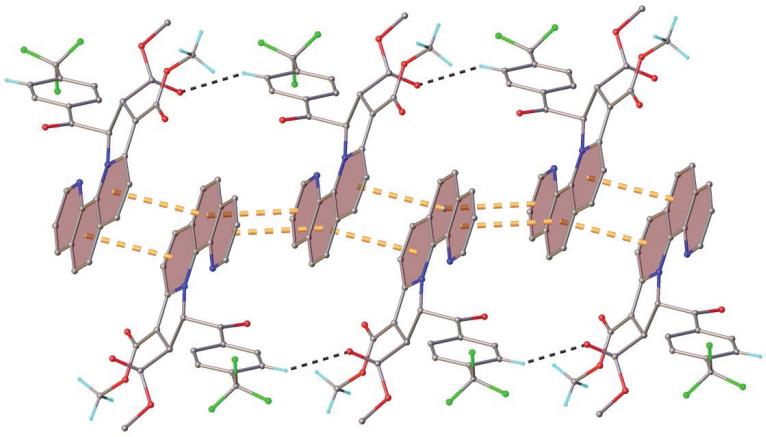


Fig. 1. X-ray molecular structure of compounds: **4b** (a) as (14S, 15S), **6a** (b) as (15R), **6b** (c) as (15S) and **7b** (d) as (12R, 13R, 14S, 15S) enantiomers with atom labelling and thermal ellipsoids at 50 % level.

Further investigation of the crystal structures packing revealed the presence of one-dimensional arrays of the neutral molecules determined by C–H···O intermolecular hydrogen bonding along with π–π stacking interactions in **4b** and **6a** (Figs. 2 and 3). In the absence of π–π stacking, the supramolecular chains in **6b** and **7b** (Figs. 4 and 5) were formed due to C–H···N (for **6b**) and C–H···N and C–H···O hydrogen bonds (for **7b**), respectively.

Photophysical investigations

The electronic absorption spectra of 1,10-phenanthroline derivatives exhibited three main absorption bands located in the following domains: 350–410 nm (α band), 295–325 nm (p band) and 250–280 nm (β band), Fig. 6. All electronic absorption spectra kept still up the fine structure, specific for the phenanthrene spectrum.[42] The nature of the (di-, tetra)hydropyrrole ring together with that if its substituents exerted an important influence on the position of the absorption and the emission bands of phenanthroline derivatives. Thus, the presence of CN or COOMe groups in position C-3 of the pyrrole like moiety resulted in a blue shift of the absorption and emission bands of phenanthroline derivatives (**4** and **7**). Moreover, the unique insertion of a CN group at C-3 position only, or in duplicate, in C-2 and C-3 positions of the (di-, tetra)hydropyrrole ring of compounds **7a** and **b** promoted the appearance of a new absorption band at 530 nm. The replacement of fluorine atom in compounds **3a**–**7a** with trifluoromethyl group in compounds **3b**–**7b** led to an increase as tenfold of the absorbance.

The fluorescence spectra of 1,10-phenanthroline derivatives **3**–**7** in DMSO displayed two emission bands located around 230 and 335 nm (Fig. 7).

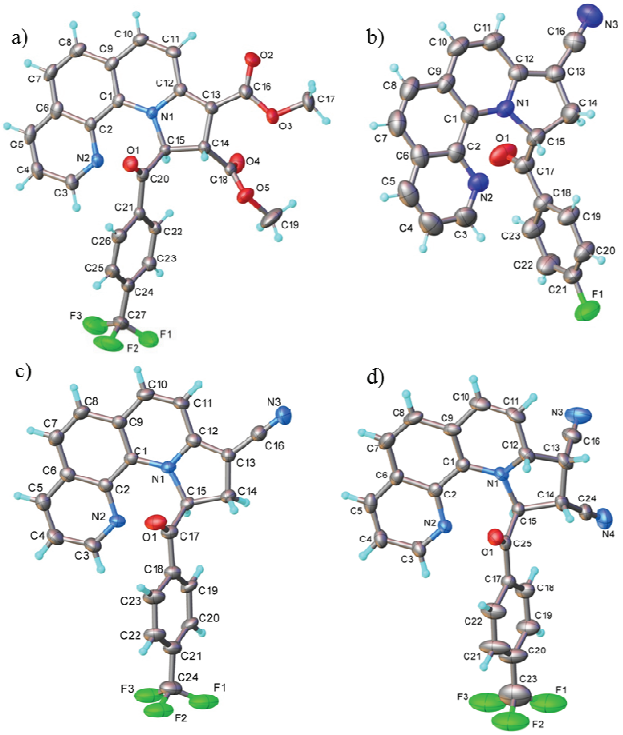


Fig. 2. The role of π-π stacking and H-bonds in the formation of 1D homochiral supramolecular array in the crystal structure of compound **4b**. H-bonds and centroid-to-centroid distances are shown as dashed black and orange lines, respectively. H-bonds parameters: 254–H···O4 [C25–H 0.95 Å, H···O4 2.47 Å, C25···O4(x, y – 1, z) 3.3295(6) Å, ∠C25HO4 145.6°].

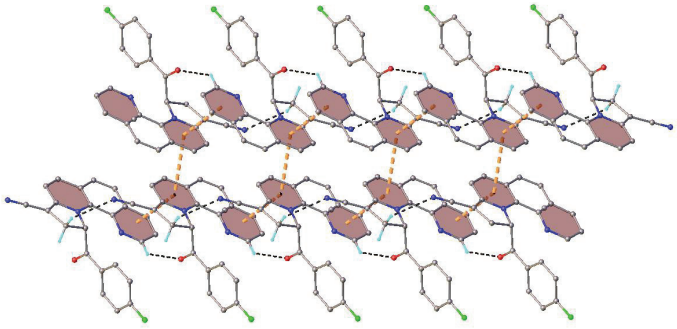


Fig. 3. The role of π-π stacking and H-bonds in the formation of 1D homochiral supramolecular array in the crystal structure of compound **6a**. H-bonds and centroid-to-centroid distances are shown as dashed black and orange lines, respectively. H-bonds parameters: C3–H···O1 [C3–H 0.93 Å, H···O1 2.43 Å, C3···O1(x, 1 + y, z) 3.166(4) Å, ∠C3HO1 135.8°]; C20–H···N3 [C20–H 0.93 Å, H···N3 2.65 Å, C20···N3(0.5 - x, 1.5 + y, 0.5 - z) 3.571(4) Å, ∠C20HN3 171.1°].

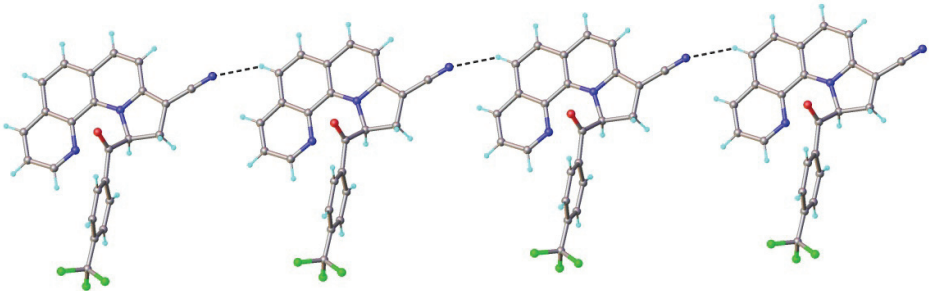


Fig. 4. One-dimensional homochiral supramolecular architecture in the crystal structure of compound **6b**. H-bond parameters: C7–H···N3 [C7–H 0.95 Å, H···N3 2.60 Å, C7···N3(*x*- 1,*y* - 1, *z*) 3.453(5) Å, ∠C7HN3 150.1°].

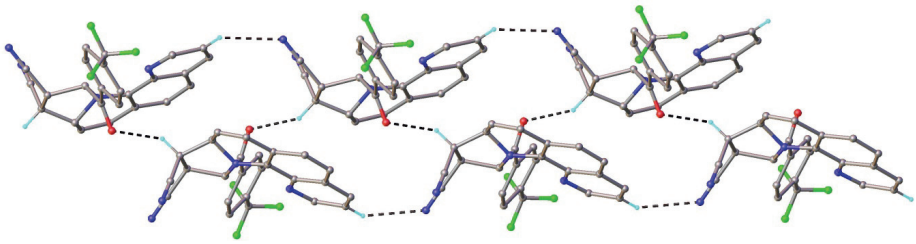


Fig. 5. One-dimensional homochiral supramolecular architecture in the crystal structure of compound **7b**. H-bonds parameters: C4–H···N4 [C4–H 0.95 Å, H···N4 2.60 Å, C4···N4(*x*, *y* – 1, *z*) 3.392(6) Å, ∠C4HN4 130.1°]; C13–H···O1 [C13–H 1.00 Å, H···O1 2.21 Å, C13···O1(-*x*, 0.5 + *y*, 0.5 - *z*) 3.042(5) Å, ∠C13HN4 139.4°].

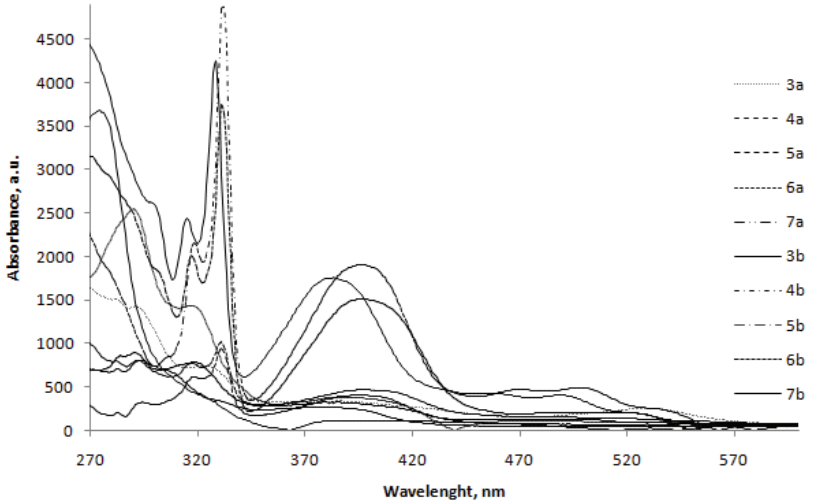


Fig. 6. UV–Vis absorption spectra in DMSO of pyrrolo[1,2-*a*][1,10]phenanthroline compounds **3**–**7**.

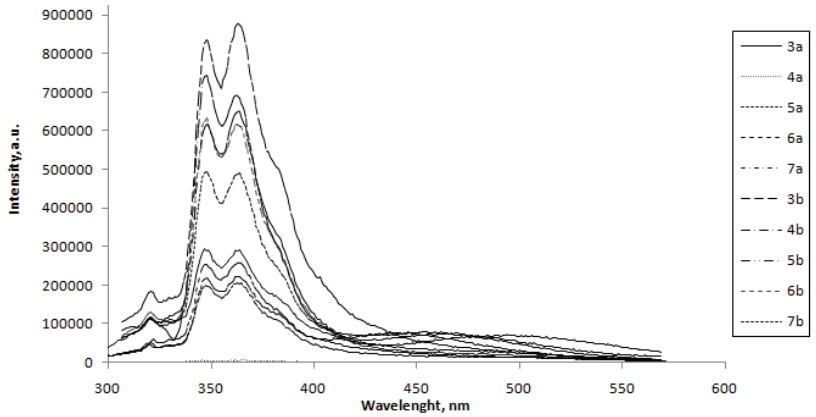


Fig. 7. Fluorescence spectra of substituted pyrrolo[1,2-*a*][1,10]phenanthroline derivatives **3**-**7a**, **b** in DMSO.

These emission bands were broad and structureless. In the case of compounds **7a** and **7b**, the appearance of a third band at about 445 nm, was also observed. As shown in Fig. 4, compound **4a** displayed no emissive properties. Usually, the fluorescence spectra of compounds with similar skeleton are substituent dependent, and in this case small differences were registered for the investigated compounds. Finally, we note the fluorescence emission being threefold increased when fluorine from compound **3-7a** was replaced with trifluoromethyl group in compounds **3**–**7**.

Antimicrobial activity

Our group has previously reported several 1,10-phenanthrolinium monoquaternary salts[7], possessing antibacterial and antifungal activities. Within this context, we tested all synthesized compounds **3**–**7** against both Gram-positive *S. Aureus* and Gram-negative *E. coli* strains, but also against *C. albicans* fungus. The antimicrobial evaluation revealed that only compounds **3a, b** proved antimicrobial activity, especially compound **3b** against the yeast strain represented by *C. Albicans* (up to 45 mm of inhibition zone). The minimum inhibitory concentration (*MIC*) values for compound **3b** were 3.125 mg/ml against *S. Aureus* and *C. Albicans* and 6.25 mg/ml against *E. coli*, respectively.

When compared with the control specimens, even if they proved to be efficient against *S.aureus* and *E. coli*, their activity was not better than the known antibiotic trimethoprim (TMP). In the same time compound **3b** proved to be by far more efficient in fighting *C. albicans* than the ordinary antifungal drug represented by nystatin (NS). Data on the average diameters of the inhibition zones for the tested compounds are presented in Table I. These results suggests that the chemical modification of 1,10-phenanthroline by locking one nitrogen atom *via* quaternization with *p*-(tri)fluoro(methyl)phenacyl moiety can be beneficial for

the antimicrobial activity (as we reported earlier[7]), while the locking by bridging a nitrogen atom into fused pyrrolo[1,2-*a*][1,10]phenanthroline leaded to the loss of antibacterial properties.

TABLE I. Antimicrobial activity of the controls and compounds **3a** and **b** against the references strains; **3a** did not show activity against *C. albicans* ATCC10231

c mg mL^{-1}	Diameter of inhibition zone ± *SD*, mm							
	S. aureus ATCC25923			*E. coli* ATCC25922			*C. albicans* ATCC10231	
	TMP	**3a**	**3b**	TMP	**3a**	**3b**	NS	**3b**
100	41.15±0.01	25.0±0.1	31±2	41.42±0.03	25.0±0.2	23.5±0.9	29.77±0.06	46±1
50	40.17±0.01	23.48±0.05	28.4±0.1	40.3±0.2	22.0±0.2	23.4±0.1	29.3±0.1	36.0±0.6
25	38.33±0.06	22.0±0.2	21.4±0.6	40.3±0.2	13.69±0.05	19.8±0.6	28.6±0.6	31.3±0.8
12.5	36.7±0.1	17.3±0.1	16.4±0.9	40.24±0.01	11.60±0.13	16.5±0.5	28.6±0.2	25.6±0.4
6.25	35.89±0.01	15.1±0.2	11±1	39.38±0.01	–	11±1	27.30±0.05	22.1±0.4
3.125	32.5±0.2	–	8.2±0.6	38.3±0.2	–	–	26.8±0.1	14.3±0.1

CONCLUSION

The synthesis and structure of novel fused 10,11-dihydropyrrolo[1,2-*a*]-[1,10]phenanthroline were presented. The cycloadducts were obtained *via* 3+2 dipolar-cycloaddition reactions to (un)symmetrically substituted π-deficient alkynes and alkenes as dipolarophiles. The cycloadditions to unsymmetrically substituted dipolarophiles (acrylonitrile and ethyl propiolate) occurred with complete regioselectivity, under charge control. The monocrystal X-ray diffraction analysis of (poly)chiral compounds **4b**, **6a** and **b** and **7b** proved unambiguously the compounds structure and the configuration of the (di-, tetra)hydropyrrole ring and brings remarkable information concerning lattice structure.

The absorption and emissive properties of (di)hydropyrrolo[1,2-*a*][1,10]phenanthroline derivatives in DMSO were substituent dependent and the introduction of trifluoromethyl substituent in benzoyl *para*-position led to a significant increase of both absorbance and emission properties. The antimicrobial activity of the synthesized compounds was measured, the salt **3b** proved to be very efficient against *S. aureus* and *C. Albicans*, with *MIC* values of 3.125 and 6.25 mg/ml, respectively.

SUPPLEMENTARY MATERIAL

Additional data and information are available electronically at the pages of journal website: https://www.shd-pub.org.rs/index.php/JSCS/article/view/9813, or from the corresponding author on request.

Acknowledgement. We thank the POSCCE-O 2.2.1, SMIS-CSNR 13984-901, Project no. 257/28.09.2010, CERNESIM, for the NMR experiments.

ИЗВОД

СИНТЕЗА И ОСОБИНЕ НОВИХ КОНДЕНЗОВАНИХ ДЕРИВАТА ПИРОЛ-1,10-ФЕНАНТРОЛИНА

CRISTINA M. AL MATARNEH[1,2], IRINA ROSCA[1], SERGIU SHOVA[1] и RAMONA DANAC[2]

[1]*"PetruPoni" Institute of Macromolecular Chemistry of Romanian Academy, 41A Grigore Ghica Voda Alley, Iasi 700487, Romania* и [2]*Chemistry Department, Faculty of Chemistry, "Al. I. Cuza" University of Iasi, 11 Carol I, Iasi 700506, Romania*

Синтетисана је нова серија деривата пирол-1,10-фенантролина у два реакциона корака, полазећи од 1,10-фенантролина и испитана је њихова антимикробна активност и флуоресцентне карактеристике. Описан синтетички приступ укључује 3+2 диполарну циклоадицију одабраних *N*-супституисаних-1,10-фенантролин-1-иум-илида, (m)етоксикарбонил и циано(1,2-ди)супституисаних ацетилена и алкена, редом. Структура синтетисаних једињења је потврђена аналитичким и спектроскопским подацима. Осим тога, молекулска структура четири одабрана једињења је одређена XRD анализом монокристала. Испитана је антимикробна активност свих синтетисаних једињења према *Staphylococcus aureus* ATCC25923, *Escherichia coli* ATCC25922 и *Candida albicans* ATCC10231.

(Примљено 19. августа 2020, ревидирано 10. јула, прихваћено 13. јула 2021)

REFERENCES

1. W. Huang, L. Wang, H. Tanaka, T. Ogawa, *Eur. J. Inorg. Chem*. **10** (2009) 1321 (https://doi.org/10.1002/ejic.200801131)
2. L. Ming, L. Xiu-Liang, W. Li-Rong, H. Zhi-Qiang, *Org. Lett.* **15** (2013) 1262 (https://doi.org/10.1021/ol400191b)
3. E. Szajdzinska-Pietek, M. Pinteala, S. Schlick, *Polymer* **45** (2004) 4113 (https://doi.org/10.1016/j.polymer.2004.03.101)
4. L. Leontie, I. Druta, R. Danac, G.I. Rusu, *Synth. Met.* **155** (2005) 138 (https://doi.org/10.1016/j.synthmet.2005.07.342)
5. M. Prelipceanu, O. S. Prelipceanu, L. Leontie, R, Danac, *Phys. Lett. A***368** (2007) 331 (http://dx.doi.org/10.1016/j.physleta.2007.04.013)
6. G. Accorsi, A. Listorti, K. Yoosaf, N. Armaroli, *Chem. Soc. Rev.* **38** (2009) 1690 (https://doi.org/10.1039/B806408N)
7. I. Druta, R. Danac, M. Ungureanu, G. Grosu, G. Drochioiu, *Ann. Pharm. Fr.* **60** (2002) 348 (https://pubmed.ncbi.nlm.nih.gov/12378146/)
8. A. Abebe, M. Atlabachew, M. Liyew, E. Ferede, *Cogent Chemistry* **4** (2018) 1476077 (https://doi.org/10.1080/23312009.2018.1476077)
9. L. Viganor, O. Howe, P. Mc Carron, M. Mc Cann, M. Devereux, *Curr. Top. Med. Chem.* **17** (2017) 1280 (https://doi.org/10.2174/1568026616666161003143333)
10. D. Wesselinova, M. Neykov, N. Kaloyanov,R.Toshkova, G. Dimitrov, *Eur. J. Med. Chem.* **44** (2009) 2720 (https://doi.org/10.1016/j.ejmech.2009.01.036)
11. L. Leontie, I. Druta, R. Danac, M. Prelipceanu, G.I. Rusu, *Prog. Org. Coat*. **54** (2005) 175 (https://doi.org/10.1016/j.porgcoat.2005.06.003)
12. A. Rotaru, R. Danac, I. Druta, G. Drochioiu, I. Cretescu, *Rev. Chim*. **56** (2005) 179 (https://revistadechimie.ro/Articles.asp?ID=570)
13. O. Gunaydin, L. Toppare, Y. Yagci, V. Harabagiu, M. Pinteala, B.C. Simionescu, *Polym. Bull.* **47(6)** (2002) 501 (https://doi.org/10.1007/s002890200014)

14. E.Maftei, C. V. Maftei, P. G. Jones, M. Freytag, M. H. Franz, G.Kelter, H.-H.Fiebig, M.Tamm, I. Neda, *Helv. Chim. Acta* **99** (2016) 469 (https://doi.org/10.1002/hlca.201500529)
15. C. V. Maftei, E. Fodor, P. G. Jones, C. G. Daniliuc, M. H. Franz, G. Kelter, H.-H. Fiebig, M. Tamm, I. Neda, *Tetrahedron* **72** (2016) 1185 (https://doi.org/10.1016/j.tet.2016.01.011)
16. L. Leontie, R. Danac, N. Apetroaei, G.I. Rusu, *Mater. Chem. Phys*. **127** (2011) 471 (https://doi.org/10.1016/j.matchemphys.2011.02.040)
17. R. Danac, L. Leontie, A. Carlescu, G. I. Rusu, *Mater. Chem. Phys*. **134** (2012) 1042 (https://doi.org/10.1016/j.matchemphys.2012.03.110)
18. I. Dhinamkaran, V. Padmini, K. Ganesan, K. Selvarasu, *Chemistry Select* **2** (2017) 6154 (https://doi.org/10.1002/slct.201700819)
19. R. Danac, A. Rotaru, G. Drochioiu, I. Druta, *J. Heterocycl. Chem.* **40** (2003) 283 (https://doi.org/10.1002/jhet.5570400213)
20. R. Danac, M. Constantinescu, A. Rotaru, A. Vlahovici, I. Cretescu, I. Druta, *Rev. Chim*. **56** (2005) 85 (https://revistadechimie.ro/Articles.asp?ID=546)
21. F. Dumitrascu, C. I. Mitan, *Tetrahedron Lett.* **42** (2001) 8379 (https://doi.org/10.1016/S0040-4039(01)01803-2)
22. M. Li, X.L. Lv, L. R. Wen, Z.Q. Hu, *Chem. Res. Chin. Univ.* **29** (2013) 1089 (https://doi.org/10.1007/s40242-013-3224-2)
23. G. Marandi, N. Hazeri, M. T. Maghsoodlou, S. M. Habibi-Khorassani, N. Akbarzadeh Torbati, F. Rostami Charati, B. W. Skelton, M. Makhad, *J. Heterocyclic Chem.* **50** (2013) 568 (https://doi.org/10.1002/jhet.1532)
24. Y. Kitahara, T. Mizuno, A. Kubo, *Tetrahedron* **60** (2004) 4283 (https://doi.org/10.1016/j.tet.2004.03.057)
25. R. Heydari, B. Tahamipour, *Chin. Chem. Lett.* **22** (2011) 1281 (https://doi.org/10.1016/j.cclet.2011.05.035)
26. C. M. Al-Matarneh, C. Ciobanu, V. Mangalagiu, G. Zbancioc, R. Danac, *Rev. Chim.* **71** (2020) 287 (https://doi.org/10.37358/RC.20.3.7998)
27. C. M. Al-Matarneh, M. O. Apostu, I. I. Mangalagiu, R. Danac, *Tetrahedron* **72** (2016) 4230 (https://doi.org/10.1016/j.tet.2016.05.061)
28. C. M. Al-Matarneh, C. Ciobanu, M. O. Apostu, I. I. Mangalagiu, R. Danac, *C. R. Chim.* **21** (2018) 1 (https://doi.org/10.1016/j.crci.2017.11.003)
29. C. M. Al-Matarneh, D.L. Isac, R. Tigoianu, R. Danac, A. Airinei, *J. Lumin.* **199** (2018) 6 (https://doi.org/10.1016/j.jlumin.2018.03.005)
30. C. M. Al-Matarneh, R. Danac, L. Leontie, F. Tudorache, I. Petrila, F. Iacomi, A. Carlescu, G. Nedelcu, I. I. Mangalagiu, *Environ. Eng. Manage. J.* **14** (2015) 420 (https://doi.org/10.30638/eemj.2015.044)
31. C. M. Al-Matarneh, S. Shova, I. I. Mangalagiu, R. Danac, *J. Enz. Inhib. Med. Chem.* **31** (2016) 470 (https://doi.org/10.3109/14756366.2015.1039530)
32. C. M. Al-Matarneh, M. C. Sardaru, M. O. Apostu, I. Rosca, C. Ciobanu, I. I. Mangalagiu, R. Danac, *Studia UBB Chemia* **LXIV** (2019) 67 (https://doi.org/10.24193/subbchem.2019.3.06)
33. C. M. Al-Matarneh, R. M. Amarandi, A. M. Craciun, I. I. Mangalagiu, G. Zbancioc, R. Danac, *Molecules* **25** (2020) 527 (https://doi.org/10.3390/molecules25030527)
34. A. Rotaru, G. Pricope, T. N. Plank, L. Clima, E. L. Ursu, M. Pinteala, J. T. Davis, M. Barboiu, *Chem. Comm.* **53** (2013) 12668 (https://doi.org/10.1039/C7CC07806D)

35. M. C. Sardaru, A. M. Craciun, C. M. Al Matarneh, I. A. Sandu, R. M. Amarandi, L. Popovici, C. I. Ciobanu, D. Peptanariu, M. Pinteala, I. I. Mangalagiu, R. Danac, *J. Enz. Inhib. Med. Chem.* **35** (2020) 1581 (https://doi.org/10.1080/14756366.2020.1801671)
36. *Rigaku Oxford Diffraction*, CrysAlisPro software system version 1.171.38.46, Rigaku Corporation, Oxford, 2015
37. O. V. Dolomanov, L. J. Bourhis, R. J. Gildea, J. A. K. Howard, H. J. Pushmann, *Appl. Crystallogr.* **42** (2009) 339 (https://doi.org/10.1107/S0021889808042726)
38. G. M. Sheldrick, *Acta Crystallogr., A* **71** (2015) 3 (https://doi.org/10.1107/S2053273314026370)
39. G. M. Sheldrick, *Acta Crystaalogr*., *C* **71** (2015) 3 (http://dx.doi.org/10.1107/S2053229614024218)
40. F. Dumitrascu, C. Draghici, M. R. Caira, L. Barbu, *Rev. Chim*. **56** (2005) 521 (https://revistadechimie.ro/Articles.asp?ID=649)
41. F. Dumitrascu, M. R. Caira, C. Draghici, M. T. Caproiu, L. Barbu, *Rev. Chim.* **60** (2009) 851 (https://revistadechimie.ro/Articles.asp?ID=2338)
42. N. S. Kozlov, K. N. Gusak, V. A. Serzhanina, L. F. Gladchenko, N. A. Krot, K. Getorotsikl, *Chem. Heterocycl. Compd*. **23** (1987) 1329 (https://doi.org/10.1007/BF00472258).