

## Article

# Synthesis and Spectroscopic Characterization of Selected Water-Soluble Ligands Based on 1,10-Phenanthroline Core

Jacek E. Nycz <sup>1,\*</sup>, Natalia Martsinovich <sup>2</sup>, Jakub Wantulok <sup>1</sup>, Tieqiao Chen <sup>3</sup>, Maria Książek <sup>4</sup>  
and Joachim Kusz <sup>4</sup>

<sup>1</sup> Institute of Chemistry, Faculty of Science and Technology, University of Silesia in Katowice, ul. Szkolna 9, 40-007 Katowice, Poland; jakub.wantulok1@gmail.com

<sup>2</sup> Department of Chemistry, University of Sheffield, Sheffield S3 7HF, UK; n.martsinovich@sheffield.ac.uk

<sup>3</sup> Ministry of Education Key Laboratory of Advanced Materials for Tropical Island Resources, Hainan Provincial Key Laboratory of Fine Chem, Hainan Provincial Fine Chemical Engineering Research Center, Hainan University, Haikou 570228, China; chentieqiao@hnu.edu.cn

<sup>4</sup> Institute of Physics, Faculty of Science and Technology, University of Silesia in Katowice, 75 Pułku Piechoty 1a, 41-500 Chorzów, Poland; maria.ksiazek@us.edu.pl (M.K.); joachim.kusz@us.edu.pl (J.K.)

\* Correspondence: jacek.nycz@us.edu.pl

**Abstract:** Water-soluble ligands based on a 1,10-phenanthroline core are relatively poorly studied compounds. Developing efficient and convenient syntheses of them would result in new interesting applications because of the importance of 1,10-phenanthrolines. In this manuscript, we describe novel and practical ways to introduce a carboxyl and, for the first time, a phenol and dithiocarboxyl group under mild reaction conditions. This strategy enables highly efficient and practical synthesis of suitable organosulfur compounds with high added value, high chemoselectivity, and a broad substrate range. We present the selective conversion of a hydroxydialdehyde in the form of 10-hydroxybenzo[*h*]quinoline-7,9-dicarbaldehyde into its derivative, unique hydroxydicarboxylic acid, by an oxidation procedure, giving 10-hydroxybenzo[*h*]quinoline-7,9-dicarboxylic acid. A similar procedure resulted in the formation of 9-methyl-1,10-phenanthroline-2-carboxylic acid by oxidation of commercially available neocuproine. An alternative method of obtaining 1,10-phenanthroline derivatives possessing carboxylic acid group can be based on the hydrolysis of ester or nitrile groups; however, this synthesis leads to unexpected products. Moreover, we apply Perkin condensation to synthesize a vinyl (or styryl) analog of 1,10-phenanthroline derivatives with phenol function. This reaction also demonstrates a new, simple, and efficient strategy for converting methyl derivatives of 1,10-phenanthroline. We anticipate that the new way of converting methyl will find wide application in chemical synthesis.

**Keywords:** phenanthroline; water-soluble ligand; dithiocarboxyl; hydroxydialdehyde; hydroxydicarboxylic acid; 10-hydroxybenzo[*h*]quinoline-7,9-dicarboxylic acid; 9-methyl-1,10-phenanthroline-2-carboxylic acid; vinyl; styryl



**Citation:** Nycz, J.E.; Martsinovich, N.; Wantulok, J.; Chen, T.; Książek, M.; Kusz, J. Synthesis and Spectroscopic Characterization of Selected Water-Soluble Ligands Based on 1,10-Phenanthroline Core. *Molecules* **2024**, *29*, 1341. <https://doi.org/10.3390/molecules29061341>

Academic Editor: Ana Margarida Gomes da Silva

Received: 21 February 2024

Revised: 12 March 2024

Accepted: 14 March 2024

Published: 18 March 2024



**Copyright:** © 2024 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (<https://creativecommons.org/licenses/by/4.0/>).

## 1. Introduction

Water-soluble ligands are widely used in various fields, including chemistry, biochemistry, and coordination chemistry. They play a crucial role in many chemical and biological processes and industrial applications, such as hydrogenation and hydrogen production from water [1], oxidation reactions [2], and hydroformylation [3,4]. The chemical and physical properties of water-soluble 1,10-phenanthroline derivatives with sulfonate, carboxylic, phosphonic acid, or hydroxylic groups in their constitution have been widely studied and used for the separation of metallic atoms and capillary electrophoresis, as well as for the development of bio-inorganic probes [5]. Furthermore, these hydrophilic groups' presence allows researchers to conduct in vitro cytotoxicity tests and assess the compounds' biological activity [6]. In addition, complexes with 1,10-phenanthroline derivatives functionalized

with sulfonate, carboxylic, phosphonic acid, or hydroxylic groups are capable of binding to metal oxide surfaces [7]. Studies have already indicated the broad scope of catalysts based on water-soluble ligands, demonstrating the industrial importance of catalyzed reactions in aqueous systems [8]. Historically, reducing molecules containing unsaturated carbon–carbon or carbon–oxygen bonds was the first application of a water-soluble catalyst [8–12]. In addition, water-soluble metal complexes have gained interesting applications in biochemistry. Some water-soluble phenanthroline complexes of rhodium, iridium, and ruthenium have found applications for the regeneration of NADH [13].

1,10-Phenanthroline is one of the most explored chelate systems among *N*-heterocyclic compounds due to its robust redox stability and a wide range of complexing properties [14,15]. These properties result from the presence of two nitrogen atoms always in a characteristic alignment in the rigid molecule structure imposed by the central benzene ring, which allows it to act as a bidentate ligand, which wraps around the metal ion, providing increased stability. 1,10-Phenanthroline can form stable complexes with various metal ions in different configurations at various oxidation states depending on conditions [16,17]. These complexes have characteristic electronic [18] and antimicrobial [19] properties, which are being continuously exploited in various fields of physics, chemistry, biology, biochemistry, crystallography, and medicine.

Water-soluble derivatives of 1,10-phenanthroline can provide many valuable applications and are important reagents for green chemistry, which is why research is essential to obtain new applications for them and new synthetic methods. So far, the water-soluble 1,10-phenanthrolines described in the chemical literature are divided into three classes: carboxylic, sulfonic, and phosphonic acid derivatives (Table 1). The described acidic 1,10-phenanthroline derivatives are bifunctional compounds that imitate amino acids or naturally occurring nicotinic acid. Unfortunately, the methods reported in the literature have many limitations, and the presented molecules are poorly characterized, especially for phosphonate and sulfonate derivatives. Sulfonate derivatives such as 4,7-diphenyl-1,10-phenanthroline disulfonic acid disodium salt or 2,9-dimethyl-4,7-diphenyl-1,10-phenanthroline disulfonic acid disodium salt are commercially available, but only as a mixture of regioisomers. There are no described synthesis procedures for the mentioned class of compounds in the literature. To the best of our knowledge, only one paper reported their NMR characteristics (only as a mixture of regioisomers) [6]. Their synthesis procedures are only presented in patent applications [20–22]. Beletskaya et al. published a synthesis method of (1,10-phenanthroline-3-yl)phosphonic acid as an example of only one phosphonate representative of acidic 1,10-phenanthroline derivative (Table 1) [23].

**Table 1.** The types of water-soluble 1,10-phenanthrolines described in the chemical literature.

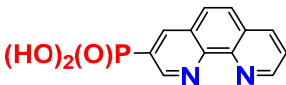
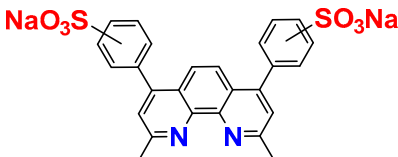
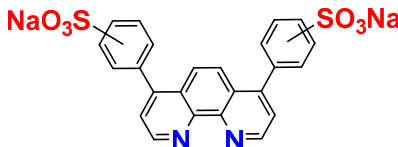
Molecule	Properties	Sources
	$^1\text{H}$ ; $^{31}\text{P}$ NMR; EA $^1$ ; procedure	[23]
	a mixture of regioisomers	commercially available
	a mixture of regioisomers	commercially available

Table 1. Cont.

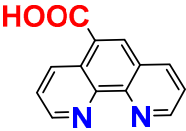
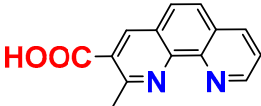
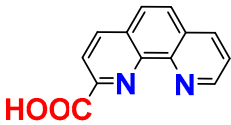
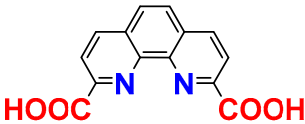
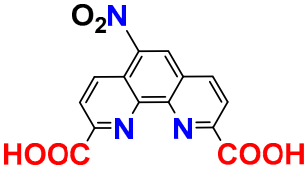
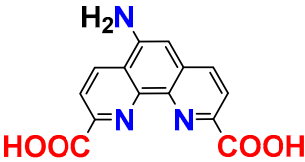
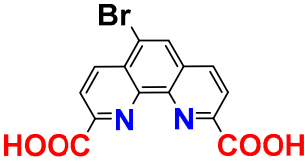
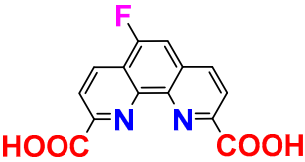
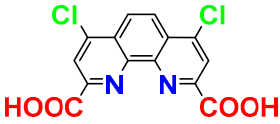
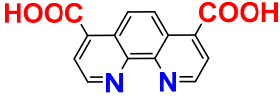
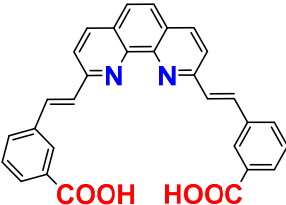
Molecule	Properties	Sources
		commercially available
	$^1\text{H}$ ; $^{13}\text{C}$ NMR; EA; procedure	[24]
	$^1\text{H}$ ; $^{13}\text{C}$ NMR; EA; procedure	[24]
	$^1\text{H}$ ; $^{31}\text{C}$ NMR; IR; mp <sup>2</sup> ; procedure $^1\text{H}$ NMR	[25] [26]
	$^1\text{H}$ NMR; MS; procedure	[24]
	patent claims	[20]
	$^1\text{H}$ ; $^{31}\text{C}$ NMR; MS; procedure	22
		[22], commercially available
	$^1\text{H}$ ; $^{31}\text{C}$ NMR; MS; mp; procedure	[27]
	$^1\text{H}$ NMR; procedure	[7]

Table 1. Cont.

Molecule	Properties	Sources
	<sup>1</sup> H NMR; procedure	[28]

<sup>1</sup> EA—Elemental analysis. <sup>2</sup> mp—melting point.

The current study presents the synthesis and spectroscopic characterization of selected water-soluble ligands based on a 1,10-phenanthroline core, rationalized based on density functional theory (DFT) calculations.

## 2. Results and Discussion

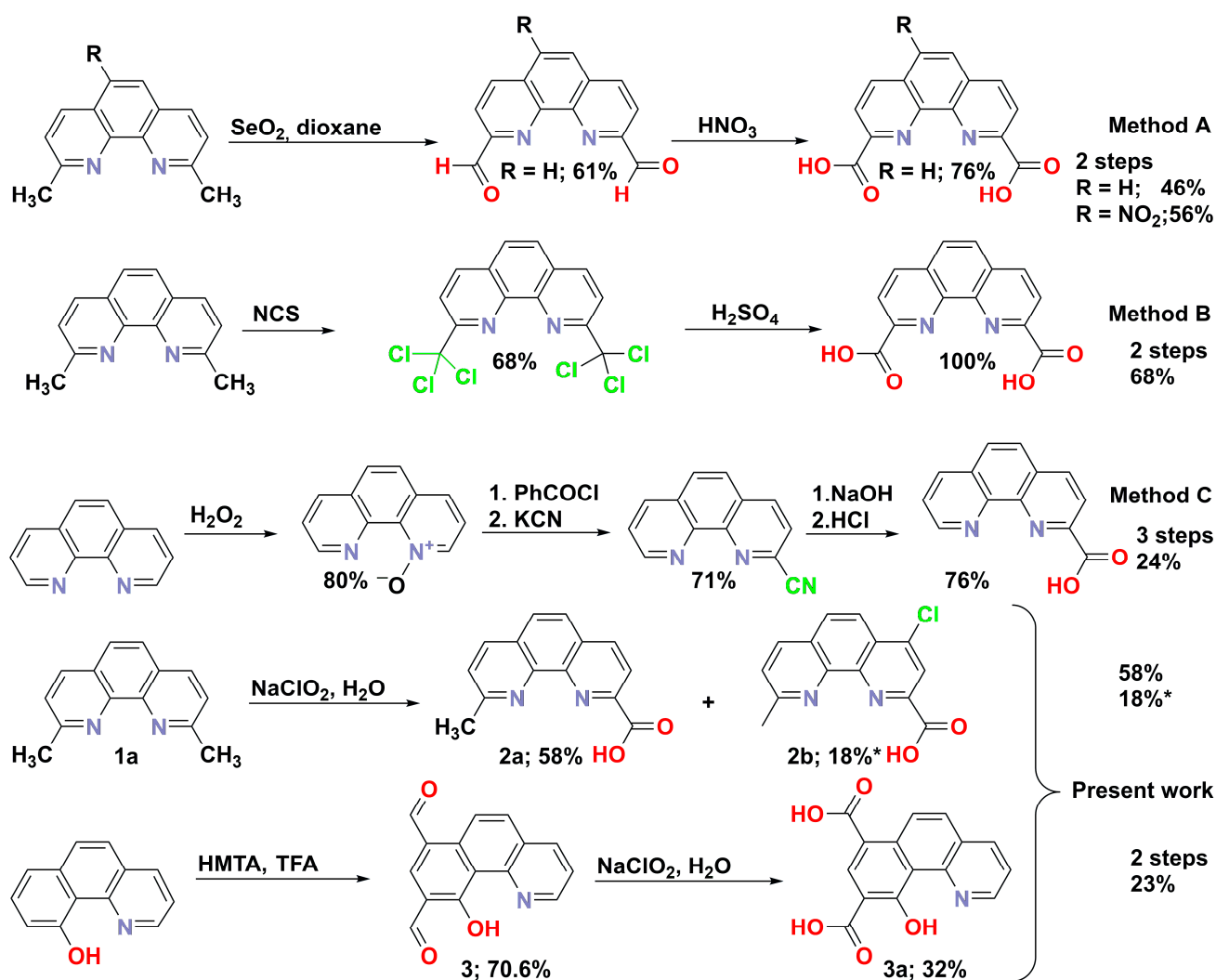
Existing publications and patents presenting the syntheses of derivatives of 1,10-phenanthroline carboxylic acid can be divided into three main methods. These are shown in Scheme 1.

Most of the previously reported syntheses of carboxylic acid derivatives of 1,10-phenanthroline are based on multi-step chemical transformations, which have the disadvantages of harsh reaction conditions and toxic materials, relatively expensive reagents or catalysts, poor product yields, long reaction times, and tedious separation procedures (Scheme 1) [7,24,27]. The inaccessibility of convenient synthetic methodologies for water-soluble 1,10-phenanthrolines is probably the most crucial reason for the lack of their applications. To meet the demand, we developed synthesis methods of selected water-soluble 1,10-phenanthrolines without employing highly toxic salts of transition metals. These methods avoid the additional handicaps of transition metals, such as the possibility of destructive oxidation of the initial 1,10-phenanthroline skeleton and contamination of the product compounds or their derivatives with transition metals, which may affect the results obtained in biological studies.

### 2.1. Synthesis of Carboxylic Acid Products by Oxidation of Methyl Groups

We develop an alternative procedure to method A presented in Scheme 1 that is based on the oxidation of commercially available 2,9-dimethyl-1,10-phenanthroline (neocuproine; **1a**) by means of sodium chlorite (Scheme 2). The reaction occurs in mild conditions in water with the use of an excess of sodium chlorite. The reaction is carried out initially at room temperature, and then the suspension is heated to reflux temperature with constant stirring for ten hours. The crucial step is the isolation of the crude product. For this purpose, the reaction mixture was carefully acidified with 10% HCl solution until the pH was acidic (pH = 2.8). This procedure was chosen based on the low cost of its implementation and the availability of reagents. As a result of the reaction, 9-methyl-1,10-phenanthroline-2-carboxylic acid (**2a**) was selectively synthesized in the case of a minor reaction scale, up to 1.0 g, with 58% yield. However, on a higher reaction scale, the reaction is more complicated (Scheme 2). We isolated and identified chlorinated products **2b** (with 18% yield), **2c**, and **2d**, similar to Miron and co-workers' results [26]. Products **2c** and **2d** were only identified by MS techniques. During the acquisition of NMR spectra in 2M water-*d*<sub>2</sub> KOD solution/DMSO-*d*<sub>6</sub>, all products showed pH-dependent regioselective isotopic H/D exchange reactions (Scheme 2). The identification of chlorinated products **2b**, **2c**, and **2d** instead of compound **2a** suggests that in the first step, the 2-methyl-9-(trichloromethyl)-1,10-phenanthroline or a similar intermediate is formed, similar to Miron et al. [26], which is further chlorinated, while in the next step, during the hydrolysis reaction, the final products are formed. During the reaction of sodium chlorite (NaClO<sub>2</sub>), hypochlorous

acid (HOCl) can be released, analogous to the Pinnick reaction. The HOCl byproduct, a reactive oxidizing agent, can also cause other side reactions with the organic starting reactant or product via a halohydrin formation reaction. The presence of molecule **2b**, **2c**, and **2d** with a chlorine atom at the C4 (or C7) position suggests a mechanism of the  $S_NAr$  type, for which no example exists in the literature. The carboxyl and methyl groups' simultaneous presence in the structure of the described acids can potentially enable further chemical transformations and allow for further functionalization.

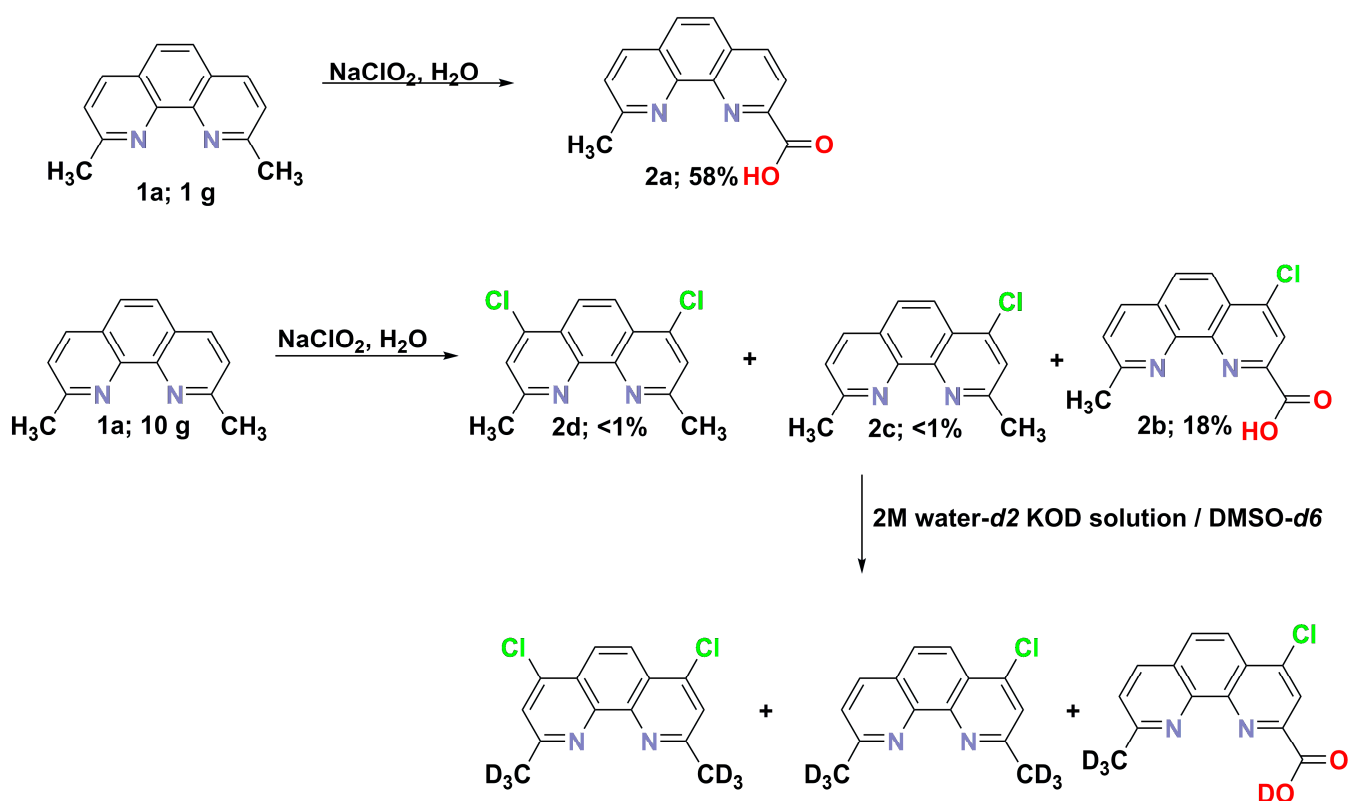


**Scheme 1.** The synthesis of 1,10-phenanthroline carboxylic acids compares literature data with present work. Method A, 46% = [R = H; [25,26]], [R = NO<sub>2</sub>; [29]] Method B [NCS (*N*-chlorosuccinimide) [23]]. Method C [30,31]. \* 10.0 g scale reaction.

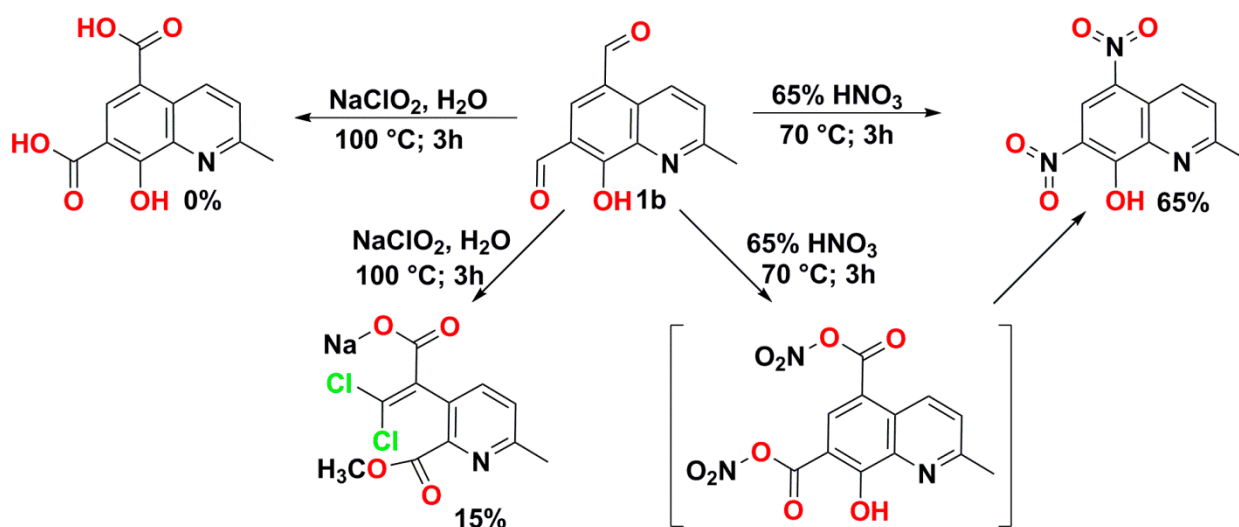
## 2.2. Oxidation of Aldehydes

We checked the effectiveness of our procedure for oxidation of selected hydroxy dialdehydes, i.e., 8-hydroxy-2-methylquinoline-5,7-dicarbaldehyde (**1b**) and 10-hydroxybenzo[*h*]-quinoline-7,9-dicarbaldehyde (**3**) (Schemes 1 and 3). Hydroxy dicarboxylic acids are an intriguing research topic, as they can be expected to participate in a variety of reactions due to the simultaneous presence of carboxyl and hydroxyl groups. Due to the site for the donor force and the excellent chelating properties associated with the presence of a hydroxyl group in the vicinity of the nitrogen atom, the compounds described can gain applications as ligands in coordination chemistry and complexometric chemical processing. The 8-hydroxy-2-methylquinoline-5,7-dicarbaldehyde (**1b**) (Scheme 3) and 10-hydroxy-

benzo[*h*]quinoline-7,9-dicarbaldehyde (**3**) (Scheme 1) were oxidized in similar reaction conditions to those in the above experiment presented in Scheme 2. The oxidation of aldehyde **3** leads to 10-hydroxybenzo[*h*]quinoline-7,9-dicarboxylic acid (**3a**) with 32% yield (Scheme 1). The aldehydes with different structures were chosen to test the possible limitations of the reaction proposed in this study. The reaction was initially carried out under mild conditions at room temperature until gas evolution ceased and then at a temperature of 100 °C. To achieve better solubility, the solvent used in the reaction was water for the quinoline derivative and formic acid for molecule **3**.



Scheme 2. Oxidation of 2,9-dimethyl-1,10-phenanthroline (neocuproine; **1a**) by sodium chlorite.



Scheme 3. Oxidation of 8-hydroxy-2-methylquinoline-5,7-dicarbaldehyde (**1b**).



The reaction of dicarbaldehyde **1b** with sodium chlorite did not lead to an expected product (Scheme 3). The reaction resulted in breaking one of the C-C bonds in the phenol ring and further side reactions that we recently described [32]. Density functional theory calculations of reactant **3** in Scheme 1 and reactant **1b** in Scheme 3 (Figure S1) showed a longer C6-C7 bond in molecule **1b** (1.410 Å) than in compound **3** (1.391 Å), potentially making the C6-C7 bond in **1b** easier to break. Calculations of the expected product (diacid) in Scheme 3 similarly showed a longer C6-C7 bond (1.408 Å) and C7-C8 bond (1.402 Å) compared to the product **3a** in Scheme 1 (1.395 and 1.396 Å, respectively), showing that these bonds in the expected product in Scheme 3 would be relatively easy to break. The obtained products were characterized by spectroscopy and mass spectrometry. These results are also consistent with the work of Miron et al. [26]. The chlorination in the C6 position in the quinoline constitution, followed by hydrolysis, can explain the ring-opening reaction.

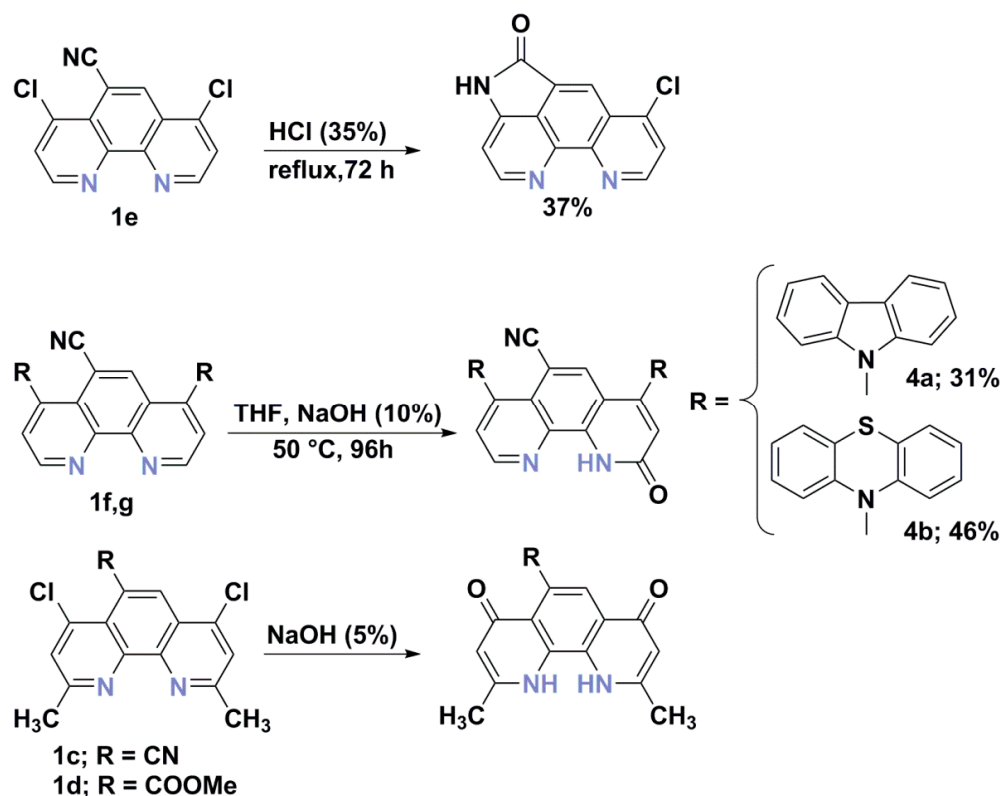
As shown above, the use of H<sub>2</sub>O<sub>2</sub> (30%) in methanol or Tollens' reagent did not allow us to obtain the target dicarboxylic acid, or the product was unstable. Therefore, we decided to use HNO<sub>3</sub>, as in earlier work by Cian et al. Hureau et al. [25,31]. Again, we did not obtain the expected product, but we obtained 2-methyl-5,7-dinitroquinolin-8-ol in 65% yield. This suggests that either each aldehyde group was oxidized by nitric acid to the carboxylic acid, which further underwent decarboxylation, and the resulting in situ 2-methylquinolin-8-ol was then nitrated, or, more likely, each aldehyde group was oxidized to nitrate ester, which underwent rearrangement (Scheme 3). It is worth mentioning that the resulting 2-methyl-5,7-dinitroquinolin-8-ol and 8-hydroxy-2-methylquinolin-5,7-dicarboxylic acid have similar *m/z* values of 249 and 247, respectively.

### 2.3. Hydrolysis of Ester- and Nitrile-Substituted Phenanthroline Compounds

Another possibility for introducing the carboxylic acid group into a 1,10-phenanthroline core can be the hydrolysis of precursors containing an ester or nitrile group. This creates a convenient opportunity for the presence of other groups suitable for further transformations. For this purpose, we hydrolyzed selected derivatives of 1,10-phenanthroline that contain either chlorine atoms or 9*H*-carbazol-9-yl and 10*H*-phenoxazin-10-yl substituents at C4 and C7 and methyl or ethyl esters or nitrile group at C5, which can be further hydrolyzed.

The 4,7-dichloro-1,10-phenanthrolines with a carboxylic acid group as substituent should be readily soluble in water. We already reported that the hydrolysis of the nitril group in 4,7-dichloro-1,10-phenanthroline-5-carbonitrile (**1e**) using an excess of hydrochloric acid leads to the formation of not the expected 4,7-dichloro-1,10-phenanthroline-5-carboxylic acid but the unexpected 7-chloropyrrolo[2,3,4-*de*][1,10]phenanthroline-5(4*H*)-one, which was isolated with 37% yield (Scheme 4) [32]. This may be attributed to the formation of a 4,7-dichloro-1,10-phenanthroline-5-amide intermediate, where the amide group, instead of being further hydrolyzed to carboxylic acid, acts as a nucleophile and attacks the nearby C4, with the chloride at C4 acting as a leaving group.

Further unexpected results were obtained during the reaction of 4,7-disubstituted-1,10-phenanthroline-5-carbonitriles (**1f,g**) in an alkaline water environment (Scheme 4). The 4,7-di(9*H*-carbazol-9-yl)-1,10-phenanthroline-5-carbonitrile (**1f**) and 4,7-di(10*H*-phenothiazine-10-yl)-1,10-phenanthroline-5-carbonitrile (**1g**) transform selectively to 4,7-di(9*H*-carbazol-9-yl)-9-oxo-9,10-dihydro-1,10-phenanthroline-5-carbonitrile (**4a**) and 9-oxo-4,7-di(10*H*-phenothiazine-10-yl)-9,10-dihydro-1,10-phenanthroline-5-carbonitrile (**4b**) (Scheme 4). We hypothesize that these products were formed through a reaction of oxidative nucleophilic substitution of hydrogen (ONSH) of the type S<sub>N</sub>ArH, with the hydroxide ion as a nucleophile in the presence of air as an oxidized reagent. In both cases, hydroxide ions attack only at C9 rather than at the C2 position. The preference for the C9 site may be explained by the difference in charges on atoms C2 and C9, caused by the non-symmetric position of the CN group: according to the DFT calculations, Mulliken charges on C9 are slightly more positive than those on C2 (by 0.01–0.004 e) both in molecules **1f** and in **1g**, making the C9 position slightly more susceptible to nucleophilic attack.



Scheme 4. Hydrolysis reactions of selected 1,10-phenanthrolines [32].

The hydrolysis reaction of 4,7-dichloro-2,9-dimethyl-1,10-phenanthroline-5-carbonitrile (**1c**) or methyl 4,7-dichloro-2,9-dimethyl-1,10-phenanthroline-5-carboxylate (**1d**) in an alkaline environment leads to their precursor 4,7-dioxo-1,4,7,10-tetrahydro-1,10-phenanthroline-5-carbonitrile or methyl 2,9-dimethyl-4,7-dioxo-1,4,7,10-tetrahydro-1,10-phenanthroline-5-carboxylate, respectively (Scheme 4). The chlorine atoms in the C4 and C7 positions are activated and easily substituted with hydroxyl in the alkaline environment. The work of J. King-Underwood et al. similarly presents reactions in the alkaline environment where the hydrolysis of the chlorine atom occurs [33].

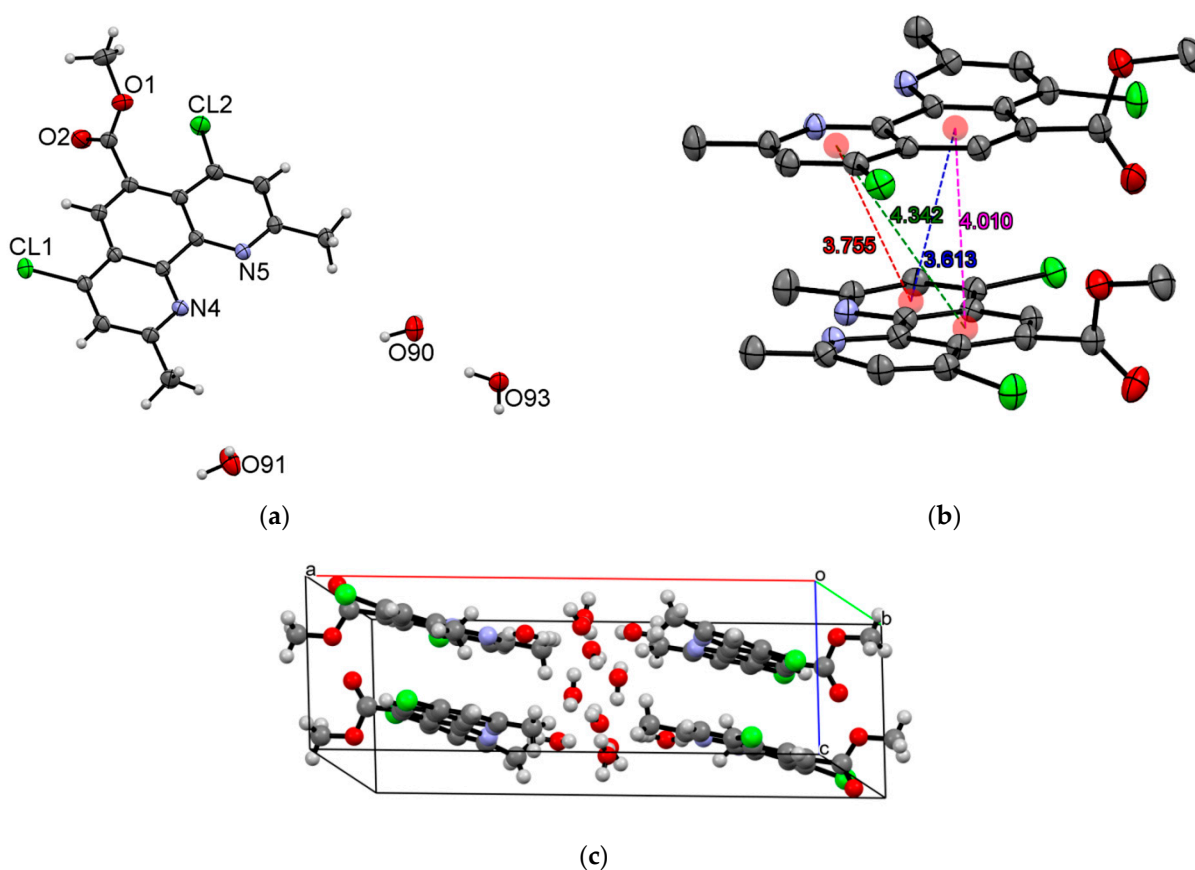
Methyl 4,7-dichloro-2,9-dimethyl-1,10-phenanthroline-5-carboxylate (**1d**) crystallizes in the monoclinic system,  $P21/c$ , with unit cell dimensions of  $a = 21.0882(6)$  Å,  $b = 11.6270(3)$  Å,  $c = 7.0683(2)$  Å,  $V = 1728.66(8)$  Å<sup>3</sup>, and  $Z = 4$ ; the monoclinic angle ( $\beta$ ) is  $94.101(3)^\circ$ , and the unit cell contains four molecules of ester and twelve of water (Figure 1c). The distance between the centroids of the phenyl and pyridine rings is in the range of 3.755 to 4.342 Å (Figure 1b).

#### 2.4. Synthesis of Dithiocarboxyl Derivatives

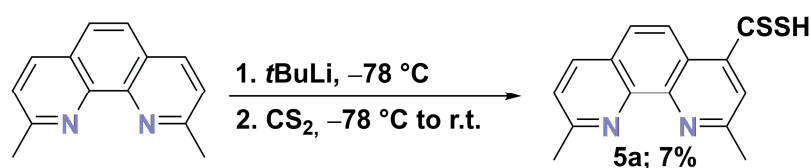
The introduction of a dithiocarboxyl group into a 1,10-phenanthroline core is unknown in the chemical literature. We report it here for the first time (Scheme 5). We presented only products with newly formed C4-CSSH bonds. The attempts to isolate other products with CH<sub>2</sub>-CSSH bonds in pure form for analytical measurements were unsuccessful. The largest difference in C-13 NMR spectroscopy is visible by comparing the carboxylic group of molecules **2a**, **2b**, and **3a** and the dithiocarboxylic group for dithiocarboxylic acid **5a**. Similarly to our previous paper [34,35], we observed an “unusual” chemical shift of 248 ppm for the dithiocarboxylic acid group of 2,9-dimethyl-1,10-phenanthroline-4-carbodithioic acid (**5a**). Density functional calculations of C-13 NMR spectra of 2,9-dimethyl-1,10-phenanthroline-4-carbodithioic acid showed the chemical shift of 243 ppm vs. TMS for the carbodithiolic carbon, in very good agreement with the experimental peak of 248 ppm. An even larger shift of 274 ppm was calculated for the carbodithiolate



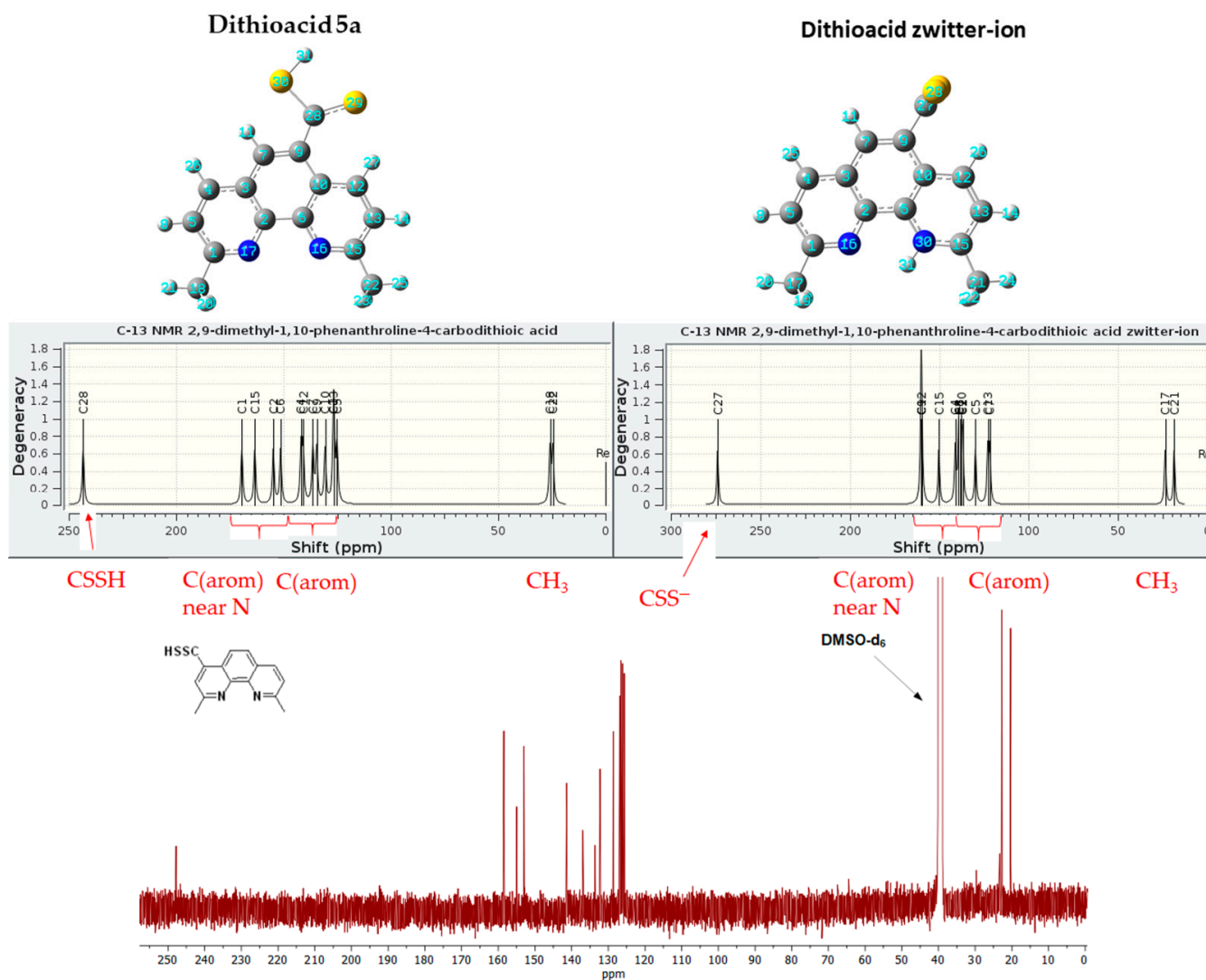
carbon in the zwitter-ion form of product **5a**. This value is much larger than the 171 ppm chemical shift calculated for the carboxylic carbon in the carboxylic acid analog. The relative deshielding of anions is observed in other cases as well. It is likely to result from an increased paramagnetic shielding contribution (the paramagnetic shielding is negative, so the nucleus is deshielded when this contribution grows), which itself is related to a decrease in the HOMO-LUMO gap. This is confirmed by our DFT calculations of molecular orbitals (Figure S2), which show a decrease in the HOMO-LUMO gap of the dithioacid (3.13 eV) compared to acid (4.31 eV, and an even smaller HOMO-LUMO gap for the zwitter-ion form of the dithioacid (1.25 eV). This change in the HOMO-LUMO gap can be attributed to changes in the localization of the frontier orbitals: in the carboxylic acid, both HOMO and LUMO are localized on the phenanthroline group, while in the dithioacid, the HOMO is localized on the thioacid group and the HOMO-1 on the phenanthroline group; in the dithioacid zwitter-ion, HOMO to HOMO-2 are on thiolate group, and HOMO-3 is on the phenanthroline group. As a result, the increased paramagnetic shielding acts as an additional magnet (Figure 2).



**Figure 1.** ORTEP (Oak Ridge thermal ellipsoid plot) drawings of methyl 4,7-dichloro-2,9-dimethyl-1,10-phenanthroline-5-carboxylate (**1d**) with 50% probability (a), the distance between centroids (b) and packing (c).



**Scheme 5.** Synthesis of dithiocarboxylic acid **5a**.

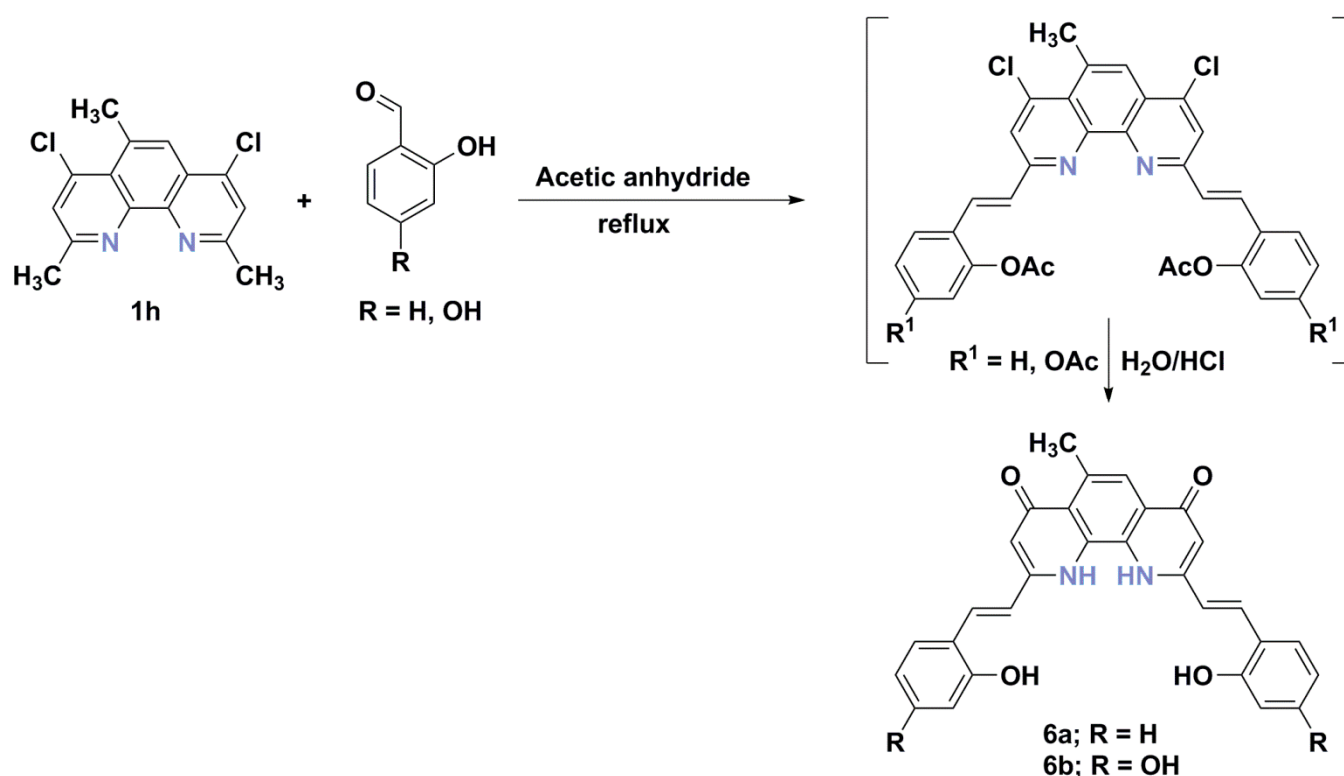


**Figure 2.** Comparison of experimental and calculated  $^{13}\text{C}\{^1\text{H}\}$ -NMR spectra of 5a.

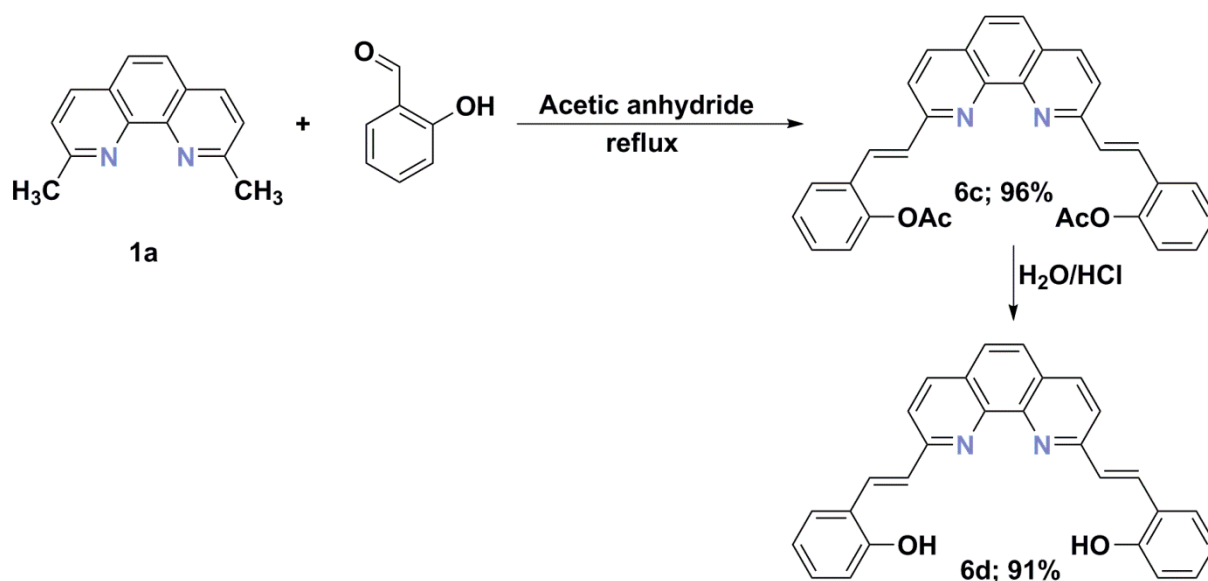
### 2.5. Synthesis of Vinyl Derivatives

The synthesis of vinyl analogs of 1,10-phenanthroline derivatives could be an alternative solution to introducing hydrophilic functions such as phenol or carboxylic acid groups. In the literature, only a few papers deal with the synthesis of vinyl analogs of 1,10-phenanthroline [28,36]. Kathirgamanathan et al. efficiently obtained four analogs as electron-transporting materials in organic light-emitting diodes (OLEDs). In a series of experiments, we apply Perkin condensation to get four vinyl analogs of 1,10-phenanthroline, which also possess phenol groups (Scheme 6). The synthetic procedure was based on our early work [37,38].

The 4,7-dichloro-1,10-phenanthrolines are sensitive to hydrolysis, which we mentioned above. This can explain why, during the synthesis of vinyl analogs of molecule 1h, we obtain 5-methyl-1,10-dihydro-1,10-phenanthroline-4,7-dione derivatives 6a and 6b, which possess the carbonyl group instead of chloride atom. Wanting to avoid a hydrolysis reaction of chloride atoms located in the C4 and C7 positions, in the next experiment, we chose neocuproine 1a as a simpler model (Scheme 7). We efficiently obtained styryl 6d and its precursor 6c by employing a straightforward and effective procedure.



Scheme 6. Synthesis of vinyl analogs of 1,10-phenanthroline.



Scheme 7. Synthesis of 2,2'-(1E,1'E)-(1,10-phenanthroline-2,9-diyl)bis(ethene-2,1-diyl)diphenol (6d).

### 3. Materials and Methods

#### 3.1. Materials

All experiments were carried out in an atmosphere of dry argon, and flasks were flame dried. Solvents were dried by usual methods (diphenyl ether, diethyl ether, and THF over benzophenone ketyl,  $\text{CHCl}_3$ , and  $\text{CH}_2\text{Cl}_2$  over  $\text{P}_4\text{O}_{10}$ , hexane, and pyridine over sodium-potassium alloy) and distilled. Chromatographic purification was carried out on silica gel 60 (0.15–0.3 mm, Macherey-Nagel GmbH & Co. KG, Dueren, Germany). Carbon disulfide ( $\text{CS}_2$ ), 2,9-dimethyl-1,10-phenanthroline (neocuproine), 2,4-dihydroxybenzaldehyde, 2-hydroxybenzaldehyde, silver nitrate ( $\text{AgNO}_3$ ), *t*BuLi (1.7 M in pentane), and sodium

chlorite ( $\text{NaClO}_2$ ) were purchased from Sigma–Aldrich (Poznań, Poland) and were used without further purification. Synthesis of 8-hydroxy-2-methylquinoline-5,7-dicarbaldehyde and 10-hydroxybenzo[*h*]quinoline-7,9-dicarbaldehyde followed our procedure described in the literature [39].

### 3.2. Instrumentation

NMR spectra were obtained with Avance 400 and 500 spectrometers (Bruker, Billerica, MA, USA) operating at 500.2 or 400.2 MHz ( $^1\text{H}$ ) and 125.8 or 100.6 MHz ( $^{13}\text{C}$ ) and 202.47 ( $^{31}\text{P}$ ) at 21 °C. Chemical shifts were referenced to ext. TMS (tetramethylsilane) ( $^1\text{H}$ ,  $^{13}\text{C}$ ) or 85%  $\text{H}_3\text{PO}_4$  ( $^{31}\text{P}$ ), or using the residual  $\text{CHCl}_3$  signal ( $\delta_{\text{H}}$  7.26 ppm) and  $\text{CDCl}_3$  ( $\delta_{\text{C}}$  77.1 ppm) as internal references, and ext. DSS for  $^1\text{H}$  and  $^{13}\text{C}$ -NMR, respectively. Coupling constants are given in Hz. The LCMS-IT-TOF analysis was performed on an Agilent 1200 Series binary LC system coupled to a micrOTOF-Q system mass spectrometer (BrukerDaltonics, Bremen, Germany). High-resolution mass spectrometry (HRMS) measurements were performed using a Synapt G2-Si mass spectrometer (Waters, New Castle, DE, USA) equipped with an ESI source and quadrupole-time-of-flight mass analyzer. To ensure accurate mass measurements, data were collected in centroid mode, and mass was corrected during acquisition using leucine enkephalin solution as an external reference (Lock-Spray) (Waters, New Castle, DE, USA). The measurement results were processed using the MassLynx 4.1 software (Waters, Milford, MA, USA) incorporated within the instrument. A Nicolet iS50 FTIR spectrometer was used to record spectra in the IR range of 4000–400  $\text{cm}^{-1}$ . FTIR spectra were recorded on a Perkin Elmer (Schwerzenbach, Switzerland) spectrophotometer in the spectral range of 4000–450  $\text{cm}^{-1}$  with the samples in the form of KBr pellets. Elementary analysis was performed using a Vario EL III apparatus (Elementar, Langenselbold, Germany). Differential scanning calorimetry (DSC) measurements were performed using a Q2000 calorimeter (TA Instruments, New Castle, DE, USA) in a nitrogen stream at a scanning rate of 10 °C/min. Samples were analyzed in aluminum pans in the temperature range of 50 to 350 °C. Melting points were determined on an MPA100 OptiMelt melting point apparatus (Stanford Research Systems, Sunnyvale, CA, USA) and were uncorrected. UV/Vis absorption spectra were measured on a SHIMADZU (Tokyo, Japan) UV-VIS-NIR spectrophotometer using quartz (Suprasil) cuvettes (10 mm path length). Fluorescence spectra were recorded on an FLS-900 spectrofluorimeter (Edinburgh Instruments, Edinburgh, UK) and were measured in quartz (Suprasil) cuvettes (10 mm path length) at 25 °C. The phosphorescence spectrum was recorded on an FLS-900 spectrofluorimeter (Edinburgh Instruments, Edinburgh, UK) at 77 K using a 3 mm (inner diameter) quartz tube inside a quartz liquid nitrogen Dewar flask.

### 3.3. X-ray Diffraction Experiments

The data for **1d** were collected using a SuperNova diffractometer (Agilent Technologies, Santa Clara, CA, USA, currently Rigaku Oxford Diffraction). Accurate cell parameters were determined and refined using the CrysAlis<sup>Pro</sup> program [40]. Also, the integration of the collected data was performed with this program. The structure was solved using direct methods with the SHELXS-2013 program and then refined using the SHELXL-2019/2 program [41]. Nonhydrogen atoms were refined with anisotropic displacement parameters. The hydrogen atoms were fixed at calculated distances and allowed to ride on the parent atoms with  $U_{\text{iso}}(\text{H})$  equal to  $1.2U_{\text{eq}}(\text{C})$  or  $1.5U_{\text{eq}}(\text{C})$ . Details concerning the determination of crystal structure are gathered in Table 2. CCDC 2298150 contains the supplementary crystallographic data for this paper.

### 3.4. Synthesis of 9-Methyl-1,10-phenanthroline-2-carboxylic Acid (**2a**). 1.0 g Scale

Molecule **1a** (1.0 g, 4.8 mmol) was added to a solution of  $\text{NaClO}_2$  (5.0 g, 55.6 mmol) in 50 mL of water at room temperature. Then, the temperature was increased to 90 °C. After carrying out the reaction for 6 h at this temperature, the resulting solution was acidified very slowly to pH 2.8 by adding HCl solution (10%). The water was then evaporated

under reduced pressure, and the crude product was extracted with MeOH and purified by Soxhlet extraction (MeOH). After the concentration of MeOH, the product was washed with CH<sub>2</sub>Cl<sub>2</sub> and finally dried over P<sub>4</sub>O<sub>10</sub>.

**Table 2.** Crystallographic data for the crystal structure of molecule **1d**.

T/K	200
CCDC number	2298150
Chemical formula	C <sub>16</sub> H <sub>18</sub> Cl <sub>2</sub> N <sub>2</sub> O <sub>5</sub>
Formula mass	389.22
Crystal system	Monoclinic
Space group	P 2 <sub>1</sub> /c
Z	4
Unit cell dimensions	
<i>a</i> /Å	21.0882(6)
<i>b</i> /Å	11.6270(3)
<i>c</i> /Å	7.0683(2)
$\beta$ /°	94.101(3)
Unit cell volume/Å <sup>3</sup>	1728.66(8)
F(000)	808
<i>D</i> <sub>x</sub> (Mg m <sup>-3</sup> )	1.496
$\mu$ (mm <sup>-1</sup> )	0.406
Theta range for data collection/°	3.379 to 36.495
Completeness	theta = 25.242° 99.8%
Range of <i>h, k, l</i>	−35 ≤ <i>h</i> ≤ 34 −19 ≤ <i>k</i> ≤ 19 −11 ≤ <i>l</i> ≤ 6
No. of measured reflections	26,199
No. of independent reflections	7930
<i>R</i> <sub>int</sub>	0.0344
Data/restraints/parameters	7930/0/239
Goodness-of-fit on F <sup>2</sup>	1.046
Final <i>R</i> <sub>1</sub> values ( <i>I</i> > 2σ( <i>I</i> ))	0.0425
Final <i>wR</i> (F <sup>2</sup> ) values ( <i>I</i> > 2σ( <i>I</i> ))	0.1040
Final <i>R</i> <sub>1</sub> values (all data)	0.0692
Final <i>wR</i> (F <sup>2</sup> ) values (all data)	0.1210
Largest diff. peak and hole/eÅ <sup>3</sup>	0.438 and −0.294

**9-Methyl-1,10-phenanthroline-2-carboxylic acid (2a)** 0.66 g (2.8 mmol, 58%); m.p. > 300 °C; <sup>1</sup>H NMR (D<sub>2</sub>O/KOD; 400.2 MHz)  $\delta$  = 2.46 (s, 3H, CH<sub>3</sub>), 6.99 (bs, 2H, aromatic), 7.02 (d, <sup>3</sup>J<sub>H,H</sub> = 8.2 Hz, 1H, aromatic), 7.50 (d, <sup>3</sup>J<sub>H,H</sub> = 8.2 Hz, 1H, aromatic), 7.68–7.76 (m, 2H, aromatic), 8.41 (bs, 1H, OH); <sup>13</sup>C{<sup>1</sup>H} NMR (D<sub>2</sub>O; 100.5 MHz)  $\delta$  = 23.3, 122.2, 123.7, 124.6, 125.9, 126.8, 128.5, 136.8, 137.0, 142.0, 142.6, 151.2, 158.2, 172.4; HRMS (ESI TOF): *m/z* Calcd for C<sub>14</sub>H<sub>9</sub>N<sub>2</sub>O<sub>2</sub> (M – H)<sup>−</sup> = 237.0664, Found 237.0662; UV–vis (methanol;  $\lambda$  [nm] (log $\epsilon$ )): 314 (3.06), 275 (3.95), 230 (4.10); IR (KBr):  $\tilde{\nu}$  = 1628, 1393, 1007, 972, 835 cm<sup>−1</sup>.

#### 10.0 g scale

Molecule **1a** (10.0 g, 48.1 mmol) was added to a solution of NaClO<sub>2</sub> (50.0 g, 556.2 mmol) in 50 mL of water at room temperature. Then, the temperature was increased to 90 °C. After carrying out the reaction for 6 h at this temperature, the resulting solution was acidified very slowly to pH 2.8 by adding HCl solution (10%). The water was then evaporated under reduced pressure, and the crude product was extracted with MeOH and purified by Soxhlet extraction (MeOH). After the concentration of MeOH, the product was washed with CH<sub>2</sub>Cl<sub>2</sub> and finally dried over P<sub>4</sub>O<sub>10</sub>.

**4-Chloro-9-methyl-1,10-phenanthroline-2-carboxylic acid (2b)** 2.4 g (8.7 mmol, 18%); DSC = 67.4 °C; <sup>1</sup>H NMR (DMSO-d<sub>6</sub>/D<sub>2</sub>O/KOD; 500.2 MHz)  $\delta$  = 2.46 (s, 3H, CH<sub>3</sub>), 7.56 (d, <sup>3</sup>J<sub>H,H</sub> = 8.2 Hz,

1H, aromatic), 7.67 (d,  $^3J_{\text{H,H}} = 8.4$  Hz, 1H, aromatic), 7.97 (s, 1H, aromatic), 8.21 (d,  $^3J_{\text{H,H}} = 8.3$  Hz, 1H, aromatic), 8.43 (d,  $^3J_{\text{H,H}} = 8.4$  Hz, 1H, aromatic);  $^{13}\text{C}\{^1\text{H}\}$  NMR (DMSO- $d_6$ /D $_2$ O/KOD; 125.8 MHz)  $\delta = 24.3, 124.6, 124.7, 122.7, 125.3, 126.5, 126.6, 127.9, 128.0, 133.3, 136.2, 136.3, 143.9, 145.4, 159.5, 159.9$ ; HRMS (ESI TOF):  $m/z$  Calcd for  $\text{C}_{14}\text{H}_5\text{D}_3\text{N}_2\text{O}_2\text{Cl}$  ( $\text{M} - \text{H}$ ) $^- = 274.0463$ , Found 274.0466.

#### Oxidation of selected dicarbaldehydes

To a solution of the appropriate hydroxy dicarbaldehyde **1b** or **3**, respectively (1.0 mmol), in water (25 mL) (formic acid for molecule **3**), a solution of  $\text{NaClO}_2$  (5.00 g, 55.6 mmol) in water (25 mL) was slowly added. The reaction was stirred at room temperature for three hours and then at 90 °C for another three hours. The reaction mixture was then concentrated, and the resulting suspension was cooled. The resulting precipitate was filtered off, washed with cold water ( $3 \times 50$  mL), and air dried. The product thus obtained was further purified by crystallization from ethanol to obtain the following:

Sodium (*E*)-3,3-dichloro-2-(2-(hydroxy(methoxy)methylene)-2,3-dihydropyridin-3-yl)acrylate 0.04 g (0.15 mmol, 15.0%);  $^1\text{H}$  NMR (400.2 MHz, DMSO- $d_6$ )  $\delta = 3.59$  (s, 3H), 7.76 (dd,  $^3J_{\text{H,H}} = 4.8, 7.8$  Hz, 1H), 8.43 (dd,  $^3J_{\text{H,H}} = 1.7, ^4J_{\text{H,H}} = 7.9$  Hz, 1H), 9.02 (dd,  $^3J_{\text{H,H}} = 1.7, ^4J_{\text{H,H}} = 4.8$  Hz, 1H).  $^{13}\text{C}\{^1\text{H}\}$  NMR (DMSO- $d_6$ ; 100.6 MHz)  $\delta = 54.02, 86.56, 90.31, 125.80, 126.89, 134.74, 158.31, 165.55, 168.75, 186.75$ ; HRMS (ESI TOF):  $m/z$  Calcd for  $\text{C}_{10}\text{H}_8\text{Cl}_2\text{NNaO}_4$  ( $\text{M}$ ) $^+ = 298.9728$ , Found 299.9632.

10-Hydroxybenzo[*h*]quinoline-7,9-dicarboxylic acid (**3a**) yellowish, 0.09 g (0.32 mmol, 32.4%); m.p.<sub>dec.</sub> = 235–245 °C;  $^1\text{H}$  NMR (DMSO- $d_6$ ; 400.2 MHz; 60 °C)  $\delta = 8.13$  (t,  $^3J_{\text{H,H}} = 7.0$  Hz, 1H, aromatic), 8.24 (d,  $^3J_{\text{H,H}} = 9.5$  Hz, 1H, aromatic), 8.94 (s, 1H, aromatic), 9.07 (d,  $^3J_{\text{H,H}} = 8.0$  Hz, 1H, aromatic), 9.24 (d,  $^3J_{\text{H,H}} = 5.4$  Hz, 1H, aromatic), 9.36 (d,  $^3J_{\text{H,H}} = 9.4$  Hz, 1H, aromatic), 16.21 (s, 1H, OH);  $^{13}\text{C}\{^1\text{H}\}$  NMR (DMSO- $d_6$ ; 100.6 MHz; 60 °C)  $\delta = 112.2, 113.2, 113.4, 122.2, 126.1, 127.6, 128.1, 137.5, 138.3, 141.3, 142.1, 143.1, 167.5, 167.8, 172.6$ ; HRMS (ESI TOF):  $m/z$  Calcd for  $\text{C}_{15}\text{H}_9\text{NO}_5\text{Na}$  ( $\text{M} + \text{Na}$ ) $^+ = 306.0378$ , Found 306.0388; UV-vis (methanol;  $\lambda$  [nm] (log $\epsilon$ )): 322 (3,96), 308 (4,03), 255 (4,49), 232 (4,84), 220 (4,85); IR (KBr):  $\tilde{\nu} = 2928, 1718, 1678, 1514, 1464, 1245, 846$   $\text{cm}^{-1}$ .

#### Synthesis of 8-hydroxy-2-methylquinoline-5,7-dicarboxylic acid

A solution of 8-hydroxy-2-methylquinoline-5,7-dicarbaldehyde (**1b**) (0.6 g, 2.8 mmol) in nitric acid (65%, 20 mL) was heated to 70 °C for three hours. The mixture was poured onto ice (ca. 40 mL), and a yellow solid precipitated. It was collected by filtration, washed with water, and dried over a vacuum to yield a yellow solid (3.80 g, 86% yield). The crude material obtained was crystallized from methanol to give the following:

2-Methyl-5,7-dinitroquinolin-8-ol as a pale yellow powder 0.45 g (1.8 mmol, 65.0%);  $^1\text{H}$  NMR (DMSO- $d_6$ ; 500.2 MHz)  $\delta = 2.94$  (s, 3H, CH $_3$ ), 8.14 (d,  $^3J_{\text{H,H}} = 9.0$  Hz, 1H, aromatic), 9.21 (s, 1H, aromatic), 9.66 (d,  $^3J_{\text{H,H}} = 9.0$  Hz, 1H, aromatic);  $^{13}\text{C}\{^1\text{H}\}$  NMR (DMSO- $d_6$ ; 125.8 MHz)  $\delta = 19.9, 122.6, 125.0, 129.0, 129.3, 130.8, 137.4, 141.2, 154.9, 161.7$ ; HRMS (ESI TOF):  $m/z$  Calcd for  $\text{C}_{10}\text{H}_6\text{N}_3\text{O}_5$  ( $\text{M} - \text{H}$ ) $^- = 248.0307$ , Found 248.0309. IR (KBr): 3510; 3170; 3005; 1594; 1528; 1321; 1260.

#### Tollens reaction

To the solution composed of  $\text{AgNO}_3$  (16.9 g, 100.0 mmol) in water (100 mL),  $\text{NaOH}$  (4.0 g, 100.0 mmol) was added, and brown silver(I) oxide was precipitate. Next, aqueous ammonia (25%) was added until the precipitate was dissolved, forming diamminesilver(I), followed by the addition of 8-hydroxy-2-methylquinoline-5,7-dicarbaldehyde (1.1 g, 5.1 mmol). The reaction was stirred at room temperature for 16 h. The resulting precipitate was filtered off, washed with water ( $3 \times 50$  mL), and acidified, and the resulting precipitate was filtered off. The obtained yellow solution was evaporated. The product thus obtained was further purified by crystallization from ethanol.

The synthesis of methyl 4,7-dichloro-2,9-dimethyl-1,10-phenanthroline-5-carboxylate was based on our procedure described in the literature [32].



*Methyl 4,7-dichloro-2,9-dimethyl-1,10-phenanthroline-5-carboxylate (1d)* beige; DSC m.p. = 175.8 °C; <sup>1</sup>H-NMR (CDCl<sub>3</sub>; 500.2 MHz) δ = 2.89 (s, 3H, CH<sub>3</sub>), 2.89 (s, 3H, CH<sub>3</sub>), 3.99 (s, 3H, CH<sub>3</sub>), 7.61 (s, 1H, aromatic), 7.62 (s, 1H, aromatic), 8.29 (s, 1H, aromatic); <sup>13</sup>C{<sup>1</sup>H}-NMR (CDCl<sub>3</sub>; 125.8 MHz) δ = 25.6, 26.0, 53.2, 121.9, 123.5, 124.7, 125.7, 128.6, 141.3, 143.2, 146.6, 146.9, 160.4, 161.5, 169.3; HRMS (ESI TOF): *m/z* Calcd for C<sub>16</sub>H<sub>13</sub>N<sub>2</sub>O<sub>2</sub>Cl<sub>2</sub> (M + H)<sup>+</sup> = 335.0354, Found 335.0353.

*Synthesis of dithiocarboxylic acid (5a)*: A solution of **1a** (2.9 g, 13.9 mmol) in THF (50 mL) was cooled (−78 °C), and *t*BuLi (11.8 mL; 1.7 M solution in pentane) was added dropwise under argon. The resulting violet solution was stirred for 1 h at ca. −78 °C, and then CS<sub>2</sub> (5 mL, 6.3 g, 83.1 mmol) was added and stirred for 1 h at ca. −78 °C, and next was stirred for 16 h at r.t. The volatiles were removed in vacuo (16 mmHg). The residue was dissolved in water, acidified by a water solution of hydrochloric acid (10%), and filtered off. The crude product was dissolved in NaOH (10%) water solution and filtered off. The solution obtained was again acidified by a water solution of hydrochloric acid (10%), and the precipitate product was obtained, filtered off, and dried over P<sub>4</sub>O<sub>10</sub> to yield the following:

*2,9-Dimethyl-1,10-phenanthroline-4-carbodithioic acid (5a)* (red) 0.3 g (1.0 mmol, 7%), DSC = 204.5 °C; <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>; 500.2 MHz) δ = 2.97 (s, 3H, CH<sub>2</sub>), 3.01 (s, 3H, CH<sub>2</sub>), 7.99 (d, <sup>3</sup>J<sub>H,H</sub> = 8.4 Hz, 1H, aromatic), 8.12 (d, <sup>3</sup>J<sub>H,H</sub> = 8.9 Hz, 1H, aromatic), 8.16 (d, <sup>3</sup>J<sub>H,H</sub> = 8.9 Hz, 1H, aromatic), 8.35 (s, 1H, aromatic), 8.84 (d, <sup>3</sup>J<sub>H,H</sub> = 8.3 Hz, 1H, aromatic), 10.47 (s, SH, 1H); <sup>13</sup>C{<sup>1</sup>H} NMR (DMSO-*d*<sub>6</sub>; 125.8 MHz) δ = 20.3, 22.7, 125.6, 126.1, 126.5, 126.9, 128.6, 132.2, 133.6, 136.9, 141.4, 153.0, 155.0, 158.5, 247.8; HRMS (ESI TOF): *m/z* Calcd for C<sub>15</sub>H<sub>12</sub>N<sub>2</sub>S<sub>2</sub> (M + H)<sup>+</sup> = 285.0520, Found 285.0515;

#### Synthesis of vinyl derivatives 6.

Molecule **1a** or **1h** (5.0 mmol) was dissolved in Ac<sub>2</sub>O (100 mL), followed by the addition of 2-hydroxybenzaldehyde (2.44 g, 20.0 mmol) or 2,4-dihydroxybenzaldehyde (2.76 g, 20.0 mmol), respectively. The reaction was heated under reflux for 24 h. Then, the volatiles were removed in vacuo (16 mmHg). A water solution of hydrochloric acid (10%) was added, and the reaction mixture was stirred under further reflux for 16 h. The crude product was purified by crystallization from ethanol (or methanol) and dried over P<sub>4</sub>O<sub>10</sub> to yield the following precipitates:

*2,9-Bis((E)-2-hydroxystyryl)-5-methyl-1,10-dihydro-1,10-phenanthroline-4,7-dione (6a)* yellow <sup>1</sup>H-NMR (MeOD/KOD; 500.2 MHz) δ = 2.59 (s, 3H, CH<sub>3</sub>), 6.35 (d, <sup>3</sup>J<sub>H,H</sub> = 10.0 Hz, 1H, aromatic), 6.49 (dd, <sup>3</sup>J<sub>H,H</sub> = 5.0 Hz, 1H, aromatic), 6.70 (dd, <sup>3</sup>J<sub>H,H</sub> = 8.3 Hz, <sup>4</sup>J<sub>H,H</sub> = 1.2 Hz, 1H, aromatic), 6.84 (s, 1H, aromatic), 7.66 (d, <sup>4</sup>J<sub>H,H</sub> = 1.2 Hz, 1H, aromatic), 7.69 (dd, <sup>3</sup>J<sub>H,H</sub> = 5.5 Hz, <sup>4</sup>J<sub>H,H</sub> = 1.2 Hz, 1H, aromatic), 8.24 (d, <sup>3</sup>J<sub>H,H</sub> = 16.4 Hz, 1H, vinyl), 8.33 (d, <sup>3</sup>J<sub>H,H</sub> = 16.1 Hz, 1H, vinyl), 8.52 (s, 1H, OH), 10.22 (s, 1H, NH); <sup>13</sup>C{<sup>1</sup>H}-NMR (MeOD/KOD; 125.8 MHz) δ = 24.3, 109.5, 111.8, 113.6, 115.1, 120.1, 120.3, 121.6, 122.0, 123.3, 124.0, 125.2, 126.7, 126.9, 131.1, 131.6, 131.7, 132.1, 133.2, 139.0, 152.1, 157.6, 161.3, 167.9, 175.0, 175.6, 175.8, 182.0, 182.1; HRMS (ESI TOF): *m/z* Calcd for C<sub>29</sub>H<sub>23</sub>N<sub>2</sub>O<sub>4</sub> (M + H)<sup>+</sup> = 463.1658, Found 463.1656.

*2,9-Bis((E)-2,4-dihydroxystyryl)-5-methyl-1,10-dihydro-1,10-phenanthroline-4,7-dione (6b)* fulvous; DSC m.p. = 65.55 °C; HRMS (ESI TOF): *m/z* Calcd for C<sub>29</sub>H<sub>23</sub>N<sub>2</sub>O<sub>6</sub> (M + H)<sup>+</sup> = 495.1556, Found 495.1555.

*((1E,1'E)-(1,10-Phenanthroline-2,9-diyl)bis(ethene-2,1-diyl))bis(2,1-phenylene) bis(hydrogen carbonate) (6c)* beige; DSC m.p. = 213.97 °C; 2.4 g (4.8 mmol, 96%), <sup>1</sup>H-NMR (DMSO-*d*<sub>6</sub>; 500.2 MHz) δ = 2.45 (s, 6H, CH<sub>3</sub>), 7.25 (dd, <sup>3</sup>J<sub>H,H</sub> = 8.0 Hz, <sup>4</sup>J<sub>H,H</sub> = 1.4 Hz, 2H, aromatic), 7.39 (td, <sup>3</sup>J<sub>H,H</sub> = 7.0 Hz, <sup>4</sup>J<sub>H,H</sub> = 1.4 Hz, 2H, aromatic), 7.44 (td, <sup>3</sup>J<sub>H,H</sub> = 7.6 Hz, <sup>4</sup>J<sub>H,H</sub> = 1.6 Hz, 2H, aromatic), 7.66 (d, <sup>3</sup>J<sub>H,H</sub> = 16.3 Hz, 2H, vinyl), 7.96 (d, <sup>3</sup>J<sub>H,H</sub> = 17.3 Hz, 2H, vinyl), 8.02 (d, <sup>3</sup>J<sub>H,H</sub> = 8.7 Hz, 3H, aromatic), 8.12 (d, <sup>3</sup>J<sub>H,H</sub> = 8.4 Hz, 2H, aromatic), 8.48 (d, <sup>3</sup>J<sub>H,H</sub> = 8.3 Hz, 2H, aromatic), 10.09 (s, 1H, OH); <sup>13</sup>C{<sup>1</sup>H}-NMR (DMSO-*d*<sub>6</sub>; 125.8 MHz) δ = 20.8, 121.7, 123.3, 126.2, 126.4, 126.57, 126.62, 128.0, 128.9, 129.6, 131.1, 136.9, 145.2, 148.6, 154.7, 169.3; HRMS (ESI TOF): *m/z* Calcd for C<sub>32</sub>H<sub>25</sub>N<sub>2</sub>O<sub>4</sub> (M + H)<sup>+</sup> = 501.1814, Found 501.1806.

Molecule **6c** (5.0 mmol) was added to a water solution of hydrochloric acid (10%) and stirred under further reflux for 16 h. Next, a water solution of sodium hydroxide (10%) was added, and the red precipitate was filtered off and purified by crystallization from methanol and dried over P<sub>4</sub>O<sub>10</sub> to yield the following precipitates:

2,2'-((1*E*,1'*E*)-(1,10-Phenanthroline-2,9-diyl)bis(ethene-2,1-diyl)diphenol (**6d**) red 1.9 g (4.6 mmol, 91%), DSC m.p. = 183.50 °C; <sup>1</sup>H-NMR (DMSO-d<sub>6</sub>; 500.2 MHz) δ = 6.95 (td, <sup>3</sup>J<sub>H,H</sub> = 7.4 Hz, <sup>4</sup>J<sub>H,H</sub> = 1.2 Hz, 2H, aromatic), 7.09 (dd, <sup>3</sup>J<sub>H,H</sub> = 8.2 Hz, <sup>4</sup>J<sub>H,H</sub> = 1.2 Hz, 2H, aromatic), 7.28 (ddd, <sup>3</sup>J<sub>H,H</sub> = 8.5 Hz, <sup>3</sup>J<sub>H,H</sub> = 7.1 Hz, <sup>4</sup>J<sub>H,H</sub> = 1.7 Hz, 2H, aromatic), 7.70 (dd, <sup>3</sup>J<sub>H,H</sub> = 7.9 Hz, <sup>4</sup>J<sub>H,H</sub> = 1.7 Hz, 2H, aromatic), 8.17 (d, <sup>3</sup>J<sub>H,H</sub> = 16.4 Hz, 2H, vinyl), 8.20 (s, 2H, aromatic), 8.39 (d, <sup>3</sup>J<sub>H,H</sub> = 16.5 Hz, 2H, vinyl), 8.56 (d, <sup>3</sup>J<sub>H,H</sub> = 8.8 Hz, 2H, aromatic), 8.88 (d, <sup>3</sup>J<sub>H,H</sub> = 8.7 Hz, 2H, aromatic); <sup>1</sup>H-NMR (DMSO-d<sub>6</sub>/KOD; 500.2 MHz) δ = 6.22–6.34 (m, 2H, aromatic), 6.45 (d, <sup>3</sup>J<sub>H,H</sub> = 17.2 Hz, 1H, vinyl), 6.46 (d, <sup>3</sup>J<sub>H,H</sub> = 16.8 Hz, 1H, vinyl), 6.85–6.94 (m, 2H, aromatic), 7.37–7.40 (m, 1H, aromatic), 7.41–7.44 (m, 1H, aromatic), 7.49 (dd, <sup>3</sup>J<sub>H,H</sub> = 5.7 Hz, <sup>4</sup>J<sub>H,H</sub> = 2.1 Hz, 2H, aromatic), 7.74 (s, 2H, aromatic), 8.09 (d, <sup>3</sup>J<sub>H,H</sub> = 8.5 Hz, 2H, aromatic), 8.19 (d, <sup>3</sup>J<sub>H,H</sub> = 16.7 Hz, 2H, vinyl), 8.26 (d, <sup>3</sup>J<sub>H,H</sub> = 8.5 Hz, 2H, aromatic); <sup>13</sup>C{<sup>1</sup>H}-NMR (DMSO-d<sub>6</sub>/KOD; 125.8 MHz) δ = 112.3, 120.5, 122.1, 123.4, 125.3, 126.0, 127.2, 127.7, 131.2, 135.1, 137.3, 145.6, 159.0, 170.2; <sup>13</sup>C{<sup>1</sup>H}-NMR (DMSO-d<sub>6</sub>; 125.8 MHz) δ = 116.6, 119.6, 122.3, 122.4, 123.6, 126.4, 128.1, 129.1, 131.4, 136.8, 136.9, 140.9, 155.2, 157.1, 169.7; HRMS (ESI TOF): *m/z* Calcd for C<sub>28</sub>H<sub>21</sub>N<sub>2</sub>O<sub>2</sub> (M + H)<sup>+</sup> = 417.1603, Found 417.1598.

### 3.5. Computational Method

Density functional theory calculations were carried out with Gaussian16 software [42] using the B3LYP functional [43,44] and cc-pVTZ basis set for all atoms. Molecular orbitals were visualized using Gaussview 6.0 [45]. C-13 NMR chemical shifts were calculated with Gaussian16 using the gauge-independent atomic orbital (GIAO) method and were plotted relative to the calculated TMS reference (B3LYP/6-311 + G(2d,p)) in Gaussview.

## 4. Conclusions

The presented research has focused on synthesizing water-soluble ligands based on the 1,10-phenanthroline core. Hydrophilic properties were obtained by introducing phenol, carboxylic acid, and dithiocarboxylic acid groups. Using simple and efficient reactions, we have developed a synthetic strategy for the dithiocarboxylic acid **5a** and vinyl (other name styryl) analog **6d** previously unknown representatives of water-soluble ligands based on a 1,10-phenanthroline core. In C-13 NMR spectroscopy, we observed a chemical shift of 248 ppm for the dithiocarboxylic acid group, similar to our previous paper [34,35]. The proton transfer reactions between the pyridine and carboxylic acid, dithiocarboxylic acid, or phenol functional groups or the generally simple protonation or deprotonation of pyridine rings in the 1,10-phenanthroline constitution could be used as a pH indicator. The compounds were further characterized by analytical methods and rationalized on the basis of DFT calculations B3LYP functional.

**Supplementary Materials:** The following supporting information can be downloaded at <https://www.mdpi.com/article/10.3390/molecules29061341/s1>. Figure S1: Calculated structures and bond distances of compounds **3**, **3a** (Scheme 1) **1b** (Scheme 3) and the expected diacid product in Scheme 3. Figure S2: Structures and frontier molecular orbitals of 2,9-dimethyl-1,10-phenanthroline-4-carboxylic acid in its neutral form, and 2,9-dimethyl-1,10-phenanthroline-4-carbodithioic acid (**5a**) in its neutral and zwitter-ion form. Figures S3–S11. <sup>1</sup>H, <sup>13</sup>C{<sup>1</sup>H} NMR, MS and HRMS spectra of the compounds.

**Author Contributions:** J.E.N. and J.W. conducted the experiments. N.M. performed DFT studies and computational analysis. J.E.N., N.M. and T.C. designed the experiment project, discussed the mechanism, and wrote the manuscript. M.K. and J.K. conducted single-crystal X-ray diffraction measurements and analysis. All authors performed investigation, visualization, and manuscript writing. All authors have read and agreed to the published version of the manuscript.

**Funding:** The research activities were co-financed by the funds granted by the National Nature and Science Foundation of China (Grant Nos. 21871070, 22261015).

**Institutional Review Board Statement:** Not applicable.

**Informed Consent Statement:** Not applicable.

**Data Availability Statement:** The data set presented in this study is available in this article. Figures S1–S11: The following are available online: CCDC 2298150 for **1d** contains the supplementary crystallographic data for this paper, accessed on 28 April 2023. These data can be obtained free of charge from <http://www.ccdc.cam.ac.uk/conts/retrieving.html> (accessed on 13 June 2022) or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; Fax: (+44) 1223-336-033; or e-mail: deposit@ccdc.cam.ac.uk.

**Acknowledgments:** N.M. acknowledges the use of the Sol computer cluster in the Department of Chemistry, University of Sheffield.

**Conflicts of Interest:** The authors declare no conflicts of interest.

## Abbreviations

DFT	density functional theory
MS	mass spectrometry
ESI	electrospray ionization
HRMS	high-resolution mass spectrometry
THF	tetrahydrofuran
DMSO	dimethyl sulfoxide
DSS (NMR standard)	sodium trimethylsilylpropanesulfonate

## References

1. Jackson, M.N.; Kaminsky, C.J.; Oh, S.; Melville, J.F.; Surendranath, Y. Graphite Conjugation Eliminates Redox Intermediates in Molecular Electrocatalysis. *J. Am. Chem. Soc.* **2019**, *141*, 14160–14167. [[CrossRef](#)] [[PubMed](#)]
2. ten Brink, G.-J.; Arends, I.W.C.E.; Sheldon, R.A. Catalytic Conversions in Water. Part 21: Mechanistic Investigations on the Palladium-Catalysed Aerobic Oxidation of Alcohols in Water. *Adv. Synth. Catal.* **2002**, *344*, 365–369. [[CrossRef](#)]
3. Ru, T.; Liang, G.; Zhang, L.; Ning, Y.; Chen, F.-E. Linear Selective Hydroformylation of 2-Arylpropenes Using Water-Soluble Rh-PNP Complex: Straightforward Access to 3-Aryl-Butyraldehydes. *ChemCatChem* **2021**, *13*, 5073–5077. [[CrossRef](#)]
4. Terhorst, M.; Plass, C.; Hinzmann, A.; Guntermann, A.; Jolmes, T.; Rösler, J.; Panke, D.; Gröger, H.; Vogt, D.; Vorholt, A.J.; et al. One-pot synthesis of aldoximes from alkenes via Rh-catalysed hydroformylation in an aqueous solvent system. *Green Chem.* **2020**, *22*, 7974–7982. [[CrossRef](#)]
5. Camerel, F.; Strauch, P.; Antonietti, M.; Faul, C.F.J. Copper—Metallomesogen Structures Obtained by Ionic Self-Assembly (ISA): Molecular Electromechanical Switching Driven by Cooperativity. *Chem. Eur. J.* **2003**, *9*, 3764–3771. [[CrossRef](#)] [[PubMed](#)]
6. De Pascali, S.A.; Migoni, D.; Papadia, P.; Muscella, A.; Marsigliante, S.; Ciccarea, A.; Fanizzi, F.P. New water-soluble platinum(II) phenanthroline complexes tested as cisplatin analogues: First-time comparison of cytotoxic activity between analogous four- and five-coordinate species. *Dalton Trans.* **2006**, *42*, 5077–5087. [[CrossRef](#)] [[PubMed](#)]
7. Eberhart, M.S.; Phelan, B.T.; Niklas, J.; Sprague-Klein, E.A.; Kaphan, D.M.; Gosztola, D.J.; Chen, L.X.; Tiede, D.M.; Poluektov, O.G.; Mulfort, K.L. Surface immobilized copper(I) diimine photosensitizers as molecular probes for elucidating the effects of confinement at interfaces for solar energy conversion. *Chem. Commun.* **2020**, *56*, 12130. [[CrossRef](#)]
8. Herrmann, W.A.; Kohlpaintner, C.W. Water-Soluble Ligands, Metal Complexes, and Catalysts: Synergism of Homogeneous and Heterogeneous Catalysis. *Angew. Chem. Int. Ed. Engl.* **1993**, *32*, 1524–1544. [[CrossRef](#)]
9. Joó, F.; Beck, M.T. Formation and catalytic properties of water-soluble phosphine complexes. *React. Kinet. Catal. Lett.* **1975**, *2*, 257–263. [[CrossRef](#)]
10. Dror, Y.; Manassen, J. Hydrogenation of olefins with rhodium-phosphine complexes, having substrate and catalyst in two different immiscible phases. An alternative method for the heterogenization of a homogeneous catalyst. *J. Mol. Catal.* **1977**, *2*, 219–222. [[CrossRef](#)]
11. Joó, F.; Tóth, Z.; Beck, M.T. Homogeneous hydrogenations in aqueous solutions catalyzed by transition metal phosphine complexes. *Inorg. Chim. Acta* **1977**, *25*, L61–L62. [[CrossRef](#)]
12. Tóth, Z.; Joó, F.; Beck, M.T. Homogeneous hydrogenations in aqueous solution catalyzed by ruthenium-phosphine complexes. *Inorg. Chim. Acta* **1980**, *42*, 153–161. [[CrossRef](#)]
13. Canivet, J.; Süß-Fink, G.; Štěpnička, P. Water-Soluble Phenanthroline Complexes of Rhodium, Iridium and Ruthenium for the Regeneration of NADH in the Enzymatic Reduction of Ketones. *Eur. J. Inorg. Chem.* **2007**, *2007*, 4736–4742. [[CrossRef](#)]

14. Koning, B.; de Boer, J.H.; Meetsma, A.; Kellogg, R.M. Synthesis and complexation characteristics of phenanthroline and bipyridine diols. *Arkiwoc* **2004**, *2*, 189–205. [[CrossRef](#)]
15. Janiak, C. A critical account on  $\pi$ - $\pi$  stacking in metal complexes with aromatic nitrogen-containing ligands. *J. Chem. Soc. Dalton Trans.* **2000**, *21*, 3885–3896. [[CrossRef](#)]
16. Bhaskar, C.; Chandrasekar, S.; Mohandas, T.; Butcher, R.J. Dibromidobis(3-bromobenzyl- $\kappa$ C)(4,7-diphenyl-1,10-phenanthroline- $\kappa$ 2N,N')tin(IV). *IUCrData* **2019**, *4*, 190336. [[CrossRef](#)]
17. Zhong, K.-L.; Cao, G.Q.; Song, W.; Ni, C. Tris(1,10-phenanthroline- $\kappa$ 2N,N')cobalt(II) bis(2,4,5-tricarboxybenzoate) monohydrate. *IUCrData* **2019**, *4*, 190059. [[CrossRef](#)]
18. Starosta, R.; Puchalska, M.; Cybińska, J.; Barys, M.; Mudring, A.V. Structures, electronic properties and solid state luminescence of Cu(I) iodide complexes with 2,9-dimethyl-1,10-phenanthroline and aliphatic aminomethylphosphines or triphenylphosphine. *Dalton Trans.* **2011**, *40*, 2459–2468. [[CrossRef](#)]
19. Viganor, L.; Howe, O.; McCarron, P.; McCann, M.; Devereux, M. The Antibacterial Activity of Metal Complexes Containing 1,10-phenanthroline: Potential as Alternative Therapeutics in the Era of Antibiotic Resistance. *Curr. Top. Med. Chem.* **2017**, *17*, 1280–1302. [[CrossRef](#)]
20. Zhou, M.; Yu, L. Electronically Neutral Metal Complexes as Biological Labels. U.S. Patent 2,016,146,826, 12 February 2019.
21. Moralesda, G.O.; Fresnadillo, D.G.; De Oteyza, P.V.G.; Aranda, J.G.; Pobes, J.M.S.; Martínez, F.Á.; Quevedo, A.R. Luminescent Pigments and Their Use in Security Applications. EP2673335A1, 10 February 2012.
22. Blondel, M.; Voisset, C.; Lista, M.-J.; Fahraeus, R.; Teulade-Fichou, M.-P. Bisquinolinium Derivatives for Preventing or Treating EBV-Related Cancers. WO2018211148A1, 22 May 2018.
23. Mitrofanov, A.; Brandès, S.; Herbst, F.; Rigolet, S.; Bessmertnykh-Lemeune, A.; Beletskaya, I. Immobilization of copper complexes with (1,10-phenanthroline)phosphonates on titania supports for sustainable catalysis. *J. Mater. Chem. A* **2017**, *5*, 12216–12235. [[CrossRef](#)]
24. Yapi, A.-D.; Valentin, A.; Chezal, J.-M.; Chavignon, O.; Chaillot, B.; Gerhardt, R.; Teulade, J.-C.; Blache, Y. In Vitro and in Vivo Antitumoral Activity of Derivatives of 1,10-Phenanthroline Framework. *Arch. Pharm. Chem. Life Sci.* **2006**, *339*, 201–206. [[CrossRef](#)]
25. De Cian, A.; DeLemos, E.; Mergny, J.-L.; Teulade-Fichou, M.-P.; Monchaud, D. Highly Efficient G-Quadruplex Recognition by Bisquinolinium Compounds. *J. Am. Chem. Soc.* **2007**, *129*, 1856–1857. [[CrossRef](#)] [[PubMed](#)]
26. Miron, C.E.; Petitjean, A. An Improved Route for the Synthesis of Guanine Quadruplex Ligand Phen-DC3. *Synlett* **2018**, *29*, 1362–1366.
27. Larsen, A.F.; Ulven, T. Efficient synthesis of 4,7-diamino substituted 1,10-phenanthroline-2,9-dicarboxamides. *Org. Lett.* **2011**, *13*, 3546–3548. [[CrossRef](#)]
28. Meng, Z.; Yang, F.; Wang, X.; Shan, W.-L.; Liu, D.; Zhang, L.; Yuan, G. Trefoil-Shaped Metal–Organic Cages as Fluorescent Chemosensors for Multiple Detection of  $\text{Fe}^{3+}$ ,  $\text{Cr}_2\text{O}_7^{2-}$ , and Antibiotics. *Inorg. Chem.* **2023**, *62*, 1297–1305. [[CrossRef](#)] [[PubMed](#)]
29. Prasad, B.; Doimo, M.; Andréasson, M.; L'Hôte, V.; Chorell, E.; Wanrooij, S. A complementary chemical probe approach towards customized studies of G-quadruplex DNA structures in live cells. *Chem. Sci.* **2022**, *13*, 2347–2354. [[CrossRef](#)] [[PubMed](#)]
30. Corey, E.J.; Borrer, A.L.; Foglia, T. Transformations in the 1,10-Phenanthroline Series. *J. Org. Chem.* **1965**, *30*, 288–290. [[CrossRef](#)]
31. Drommi, M.; Rulmont, C.; Esmieu, C.; Hureau, C. Hybrid Bis-Histidine Phenanthroline-Based Ligands to Lessen A $\beta$ -Bound Cu ROS Production: An Illustration of Cu(I) Significance. *Molecules* **2021**, *26*, 7630. [[CrossRef](#)] [[PubMed](#)]
32. Nycz, J.E.; Wantulok, J.; Sokolova, R.; Pajchel, L.; Stankevič, M.; Szala, M.; Malecki, J.G.; Swoboda, D. Synthesis and electrochemical and spectroscopic characterization of 4,7-diamino-1,10-phenanthrolines and their precursors. *Molecules* **2019**, *24*, 4102. [[CrossRef](#)]
33. Hardy, G.; King-Underwood, J.; Hardy, G.; Murray, P.J.; Williams, G.J.; Onions, T.S.; Gareth, J. Pyrazole p38 Map Kinase Inhibitors. U.S. Patent 201,302,999,0A1, 31 January 2013.
34. Nycz, J.E.; Szala, M.; Malecki, G.J.; Nowak, M.; Kusz, J. Synthesis, spectroscopy and computational studies of selected hydroxyquinolines and their analogues. *Spectrochim. Acta A* **2014**, *117*, 351–359. [[CrossRef](#)]
35. Nycz, J.E.; Malecki, G.J. Synthesis, spectroscopy and computational studies of selected hydroxyquinoline carboxylic acids and their selected fluoro-, thio-, and dithioanalogues. *J. Mol. Struct.* **2013**, *1032*, 159–168. [[CrossRef](#)]
36. Kathirgamanathan, P.; Surendrakumar, S.; Vanga, R.R.; Ravichandran, S.; Antipan-Lara, J.; Ganeshamurugan, S.; Kumaravel, M.; Paramaswara, G.; Arkley, V. Arylvinylene phenanthroline derivatives for electron transport in blue organic light emitting diodes. *Org. Electron.* **2011**, *12*, 666–676. [[CrossRef](#)]
37. Nycz, J.E.; Czyż, K.; Szala, M.; Malecki, J.G.; Shaw, G.; Gilmore, B.; Jon, M. Synthesis, spectroscopy and computational studies of some novel  $\pi$ -conjugated vinyl N-alkylated quinolinium salts and their precursor's. *J. Mol. Struct.* **2016**, *1106*, 416–423. [[CrossRef](#)]
38. Gudat, D.; Nycz, J.E.; Polanski, J. A solid state and solution NMR study of the tautomerism in hydroxyquinoline carboxylic acids. *Magn. Reson. Chem.* **2008**, *46*, S115–S119. [[CrossRef](#)] [[PubMed](#)]
39. Wantulok, J.; Szala, M.; Quinto, A.; Nycz, J.E.; Giannarelli, S.; Sokolova, R.; Książek, M.; Kusz, J. Synthesis and electrochemical and spectroscopic characterization of selected quinolinecarbaldehydes and Schiff bases as their derivatives. *Molecules* **2020**, *25*, 2053. [[CrossRef](#)] [[PubMed](#)]
40. Rigaku Oxford Diffraction. *CrysAlisPro Software System, Version 1.171.38.41q*; Rigaku Corporation: Wroclaw, Poland, 2015.
41. Sheldrick, G.M. Crystal structure refinement with SHELXL. *Acta Cryst.* **2015**, *C71*, 3–8.

42. Frisch, M.J.; Trucks, G.W.; Schlegel, H.B.; Scuseria, G.E.; Robb, M.A.; Cheeseman, J.R.; Scalmani, G.; Barone, V.; Petersson, G.A.; Nakatsuji, H.; et al. *Gaussian 16, Revision C.01*; Gaussian, Inc.: Wallingford, CT, USA, 2019.
43. Becke, A.D. Density-functional exchange-energy approximation with correct asymptotic behavior. *Phys. Rev. A* **1988**, *38*, 3098–3100. [[CrossRef](#)] [[PubMed](#)]
44. Lee, C.T.; Yang, W.T.; Parr, R.G. Development of the Colle-Salvetti correlation-energy formula into a functional of the electron density. *Phys. Rev. B* **1988**, *37*, 785–789. [[CrossRef](#)] [[PubMed](#)]
45. Dennington, R.; Keith, T.A.; Millam, J.M. *GaussView, Version 6*; Semichem Inc.: Shawnee Mission, KS, USA, 2016.

**Disclaimer/Publisher’s Note:** The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.