Scientific Research Publishing

International Journal of Organic Chemistry, 2022, 12, 40-52
https://www.scirp.org/journal/ijoc
ISSN Online: 2161-4695
ISSN Print: 2161-4687

Synthesis, Characterization, Computational and Antibacterial Studies of Novel Dopamine-Based Derivatives

Michèle-L. Lieunang Watat*, Jovita S. Chi, Claudia E. Asanji, Emmanuel N. Nfor*

Department of Chemistry, Faculty of Science, University of Buea, Buea, Cameroon
Email: *lieunang.watat@ubuea.cm

How to cite this paper: Watat, M.-L.L., Chi, J.S., Asanji, C.E. and Nfor, E.N. (2022) Synthesis, Characterization, Computational and Antibacterial Studies of Novel Dopamine-Based Derivatives. *International Journal of Organic Chemistry*, **12**, 40-52.
https://doi.org/10.4236/ijoc.2022.121004

Received: February 17, 2022
Accepted: March 28, 2022
Published: March 31, 2022

Abstract

Two novel dopamine hydrochloride Schiff bases (*E*)-4-(2-((4-hydroxy-2*H*-chromen-2-ylidene)amino)ethyl)benzene-1,2-diol (**1**) and (*E*)-3-((3,4-dihydroxyphenethyl)imino)indolin-2-one (**2**) have been synthesized using isatin and 4-hydroxycoumarin. The prepared compounds have been characterized by solubility in different solvents, melting point determination, elemental analysis, FT-IR, ^{1}H-NMR, ^{13}C-NMR and powder X-ray diffraction spectroscopic techniques, with the structures of the Schiff bases proposed. The proposed structures of the compounds have been optimized using the Spartan program so as to get the most stable conformers. The synthesized Schiff bases have been tested for their biological activity against two *Gram positive bacteria*; *Staphylococcus aureus, Bacillus subtilis,* and two *Gram negative bacteria*; *Klebsiella pneumoniae* and *Escherichia coli* with their minimum inhibition concentration (MIC) values determined. The Schiff base **1** was found to inhibit *E. coli and K. pneumonia* with MIC values of 3.12 and 6.25 μg/mL, followed by *K. pneumonia* compared to the reference standards with MIC values of 3.12 μg/ml indicating that **1** could be a potential lead compound.

Keywords

Dopamine Hydrochloride, Schiff Bases, Computational, Antibacterial

1. Introduction

Dopamine (3-hydroxytyramine hydrochloride) is a biogenic monoamine which belongs to a family of neurotransmitters called "catecholamines". These catecholamines include several related neurotransmitters which are dopamine, norepinephrine also known as noradrenalin, and epinephrine also known as adrenalin [1]. These neurotransmitters are considered to be unquestionably the most rele-

vant to both normal and abnormal behavior [1]. Dopamine is a neurotransmitter that can produce a myriad of actions on neurons either directly or through G-protein-coupled receptors and is inactivated primarily through its reuptake by the dopamine transporter back into presynaptic terminals of neurons shortly after its release [1] [2]. Thus, it is not a fast-acting neurotransmitter. Dopamine is found in the kidney peripherally and has many functions or applications depending on the receptor involved. These include; voluntary movements, regulate growth and development, regulations of feeding, sleep, impulse control, reproductive behaviors, working memory, learning, control of rennin in kidney (D1), renal functions, gastrointestinal motility, regulate locomotion-presynaptic receptors inhibit locomotion and post synaptic receptors activate locomotion (D2), involved in endocrine function cognitions, emotions, regulations of locomotor functions and modulates endocrine functions (D3). Therapeutically, dopamine is indicated for the correction of hemodynamic imbalances present in the shock syndrome due to myocardial infarctions, trauma, endotoxic septicemia and open heart surgery [3].

The development of antibiotics against gram-positive and gram-negative bacteria such as *Staphylococcus aureus* (S.A), *Bacillus subtilis* (B.S), *Klebsiella pneumonia* (K.P) and *Escherichia coli* (E.C) has been an active area of research, as amoxicillin, norfloxacin, chloramphenicol and ciprofloxacin which are the most common antibiotics used for these bacterial infections are associated with side effects such as neurological alterations generated by the interaction of the drug with the central nervous system [4].

Furthermore antimicrobial agents are not only fundamental for the treatment of infections in humans, but are also essential substances in agriculture and animal husbandry, where they are applied at sub-therapeutic levels as growth promoters in birds, swine, beef and fish food [5]. The emergence of multi-resistant bacteria has become a major problem for the treatment of infectious diseases; as such there is a pressing need to search for new alternative antibiotics with ease of synthesis and with relatively fewer side effects. Most compounds bearing an azomethine group have been reported to exhibit antimicrobial [6] [7] [8], antioxidant, and antiproliferative properties [9] [10].

In view of the above, and in continuation with our studies on novel Schiff base compounds with potential antimicrobial activity [11] [12] [13], and taking into consideration the therapeutic importance of dopamine, isatin, and 4-hydroxycoumarin, we report herein the syntheses, characterization and antibacterial studies of dopamine-based derivatives of isatin and 4-hydroxycoumarin, with the view of developing new and efficient anti-microbial agents.

2. Experimental

Gallenkamp melting point apparatus containing a mercury-in-glass thermometer with a range of 10˚C to 360˚C, melting temperature capillary tubes [sizes = (1.5 - 1.8) × 90 mm]. The Fourier-transform infrared (FT-IR) spectra were rec-

orded (KBr) with a Perkin-Elmer 1430 spectrophotometer. The proton and carbon-13 nuclear magnetic resonance (NMR) spectra of **1** and **2** were recorded on Bruker DRX-500, −400, and −300 MHz instruments and calibrated on residual undeuterated solvent signals as an internal standard. The X-ray powder diffractogram of the compounds were recorded using CuKα (wave length of 1.5406) as source in the range 4 - 60˚(2θ).

2.1. Synthesis of (*E*)-4-(2-((4-hydroxy-2*H*-chromen-2-ylidene)amino)ethyl)benzene-1, 2-diol (1)

A solution of 4-hydroxycoumarin (0.324 g, 0.002 mol) dissolved in 20 mL of ethanol was added to a solution of dopamine hydrochloride (0.379 g, 0.002 mol) dissolved in 20 mL ethanol, with the addition of a few drops of glacial acetic acid into the mixture. The reaction mixture was refluxed for 6 hours at a temperature of 70˚C. On cooling, the precipitate was filtered and washed several times with ethanol and dried over $CaCl_2$ desiccator. Percentage yield 83.1%, $C_{17}H_{15}NO_4$, m/z 297.10; Analysis; Found: C, 68.61; H, 5.06; N, 4.68; O, 21.47, Calculated: C, 68.68; H, 5.09; N, 4.71; O, 21.53, mp 183˚C - 192˚C, IR 3336, 3038, 2641, 2542, 2361, 2078, 1939, 1616, 1498, 1284, 1174, 1013, 935, 813, 598 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ = 10.42 (br, 1H), 9.64 (br, 1H), 9.49 (br, 1H), 7.55 (m, 2H), 7.38 (m, 2H), 6.96 (m, 3H), 5.06 (s, 1H), 4.67 (m, 2H), 3.82 (m, 2H); ^{13}C NMR (101 MHz, DMSO-d_6) δ = 189.7, 152.9, 152.7, 146.1, 134.2, 129.3, 129.2, 125.8, 125.5, 122.3, 117.2, 115.9, 115.3, 62.5, 52.1, 45.6, 37.7.

2.2. Synthesis of (*E*)-3-((3, 4-dihydroxyphenethyl) imino) indolin-2-one (2)

A solution of Isatin (0.294 g, 0.002 mol) dissolved in 20 mL of ethanol was added to a solution of dopamine hydrochloride (0.379 g, 0.002 mol) dissolved in 20 mL ethanol, with the addition of a few drops of glacial acetic acid into the mixture. The reaction mixture was heated for 6 hours at a temperature of 70˚C. On cooling, the precipitate was filtered and washed several times with ethanol and dried over $CaCl_2$ desiccator. Percentage yield 84.3%, $C_{16}H_{14}N_2O_3$, m/z, 282.10; Analysis; Found: C, 68.04; H, 4.98; N, 9.87; O, 16.98, Calculated: C, 68.07; H, 5.00; N, 9.92; O, 17; IR 3402, 3159, 2360, 1707, 1620, 1450, 1329, 768 cm^{-1}; ^1H NMR (300 MHzDMSO-d_6) δ_H = 10.37 (br, 1H), 9.64 (br, 1H), 8.27 (s, 1H), 7.41 (m, 4H), 6.94 (m, 3H), 4.74 (s, 2H), 4.48 (s, 2H); ^{13}C NMR (101 MHz, DMSO-d_6) δ_C = 190.2, 176.5, 154.1, 152.7, 146.0, 143.0, 140.2, 134.3, 130.5, 125.6, 122.3, 115.8, 115.2, 58.6, 52.5, 41.7.

2.3. Computational Studies

Semi-empirical studies were done with Spartan'14 program [14] in gas phase using PM3 method [15]. The molecules were pre-optimized using molecular mechanics methods. Several cycles of energy minimization had to be carried out for each of the molecules. Geometry was optimized using molecular mechanics MMFF minimum energy optimization.

2.4. Antimicrobial Activity

2.4.1. Antibacterial Test for the Synthesized Schiff Bases

The *in vitro* antibacterial activity of the synthesized compounds was assessed [16] [17] against two *Gram positive bacteria*; *Staphylococcus aureus* (ATCC-12598), *Bacillus subtilis* (ATCC-6633) and two *Gram negative bacteria*; *Klebsella pneumonia* (ATCC-29665) and *Escherichia coli* (ATCC-25922) using the broth micro dilution method.

2.4.2. Preparation of Media

1) Sterilization of media and glassware

The media used was Mueller-Hinton agar (Thermo Fisher Scientific, Waltham, MA USA) and the nutrient agar was sterilized in conical flasks of a suitable capacity by autoclaving at 15 lb pressure approximately 20 minutes. The test tubes and pipettes were sterilized in hot air oven at 160˚C for one hour.

2) Preparation of test compounds

Serial dilution of the compounds and reference drugs were prepared in Mueller-Hinton agar (Thermo Fisher Scientific). Drugs (1 mg) were dissolved in dimethylsulfoxide/$CDCl_3$ (1 mL). Further, progressive dilution with the melted Mueller-Hinton agar (Thermo Fisher Scientific) were performed to obtain the required concentrations, 0.2, 0.4, 0.8, 1.6, 3.125, 6.25, 12.5, 25, 50 and 100 µg/mL of test compounds.

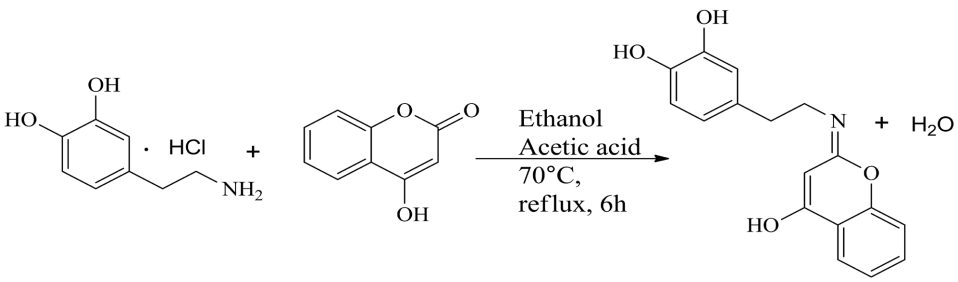
To ensure that the solvent had no effect on the bacterial growth, a control experiment was performed at the same dilution as used in the experiment. The DMSO/$CDCl_3$ did not show any effect on the micro-organism in the concentration range studied.

3. Results and Discussion

The condensation reactions between dopamine hydrochloride and 4-hydroxycoumarin and isatin gave the desired products as depicted in Scheme 1 and Scheme 2.

3.1. Elemental Analyses

The experimental and calculated values of the elemental analyses of the prepared compounds were in good agreement. The agreement between these values of the elemental analyses confirms the purity of the prepared compounds. The theoretical molecular ion peaks appeared at m/z 297.10 and 282.10 for $C_{17}H_{15}NO_4$ (**1**)



Scheme 1. Synthesis of **1**.

and $C_{16}H_{14}N_2O_3$ (**2**) respectively**.** Furthermore, the synthesized compounds were all very soluble in DMSO which is a coordinating solvent. Isatin derivative **2** was slightly soluble in methanol, while the 4-hydroxycoumarin derivative **1** was very soluble in methanol.

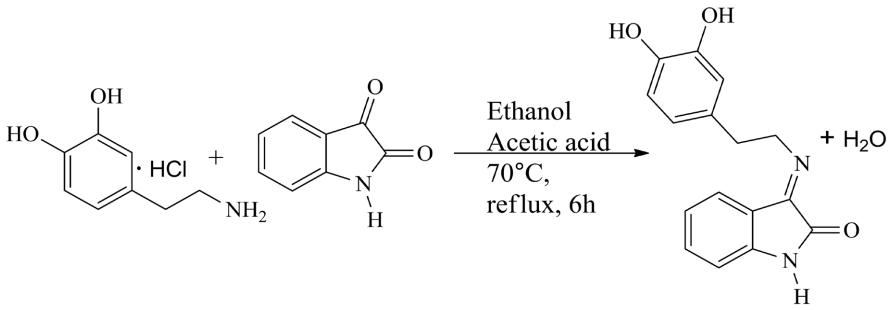
3.2. Infrared Spectra

The infrared spectra of the synthesized Schiff bases were recorded on KBr in the range 4000 - 400 cm^{-1}.

The infrared spectrum of (*E*)-4-(2-((4-hydroxy-2*H*-chromen-2-ylidene)amino)ethyl)benzene-1, 2-diol (**1**) is presented in **Figure 1**, while that of (*E*)-3-((3, 4-dihydroxyphenethyl) imino) indolin-2-one (**2**) is presented in **Figure 2**.

The spectrum of **1** displayed strong bands at 3336 and 3038 cm^{-1} corresponding to the stretching frequency vibrations of v(OH) and v(NH) respectively [18] [19]. The stretching frequency vibration of the azomethine group (C=N) of the Schiff base is observed at 1616 cm^{-1} [20] [21], while the C-O stretching vibration characteristic of this Schiff base appeared at 1284 cm^{-1} [22] [23].

For the IR spectrum of **2** (**Figure 2**), it displayed strong bands at 3402 and 3159 cm^{-1} corresponding to the OH and N-H stretching vibration respectively [18]. A strong band was seen at 1707 cm^{-1} corresponding to the C=O stretching vibration, while a sharp band at 1620 cm^{-1} is attributed to the stretching vibration of azomethine group (C=N) of the Schiff base [22].



Scheme 2. Synthesis of **2**.

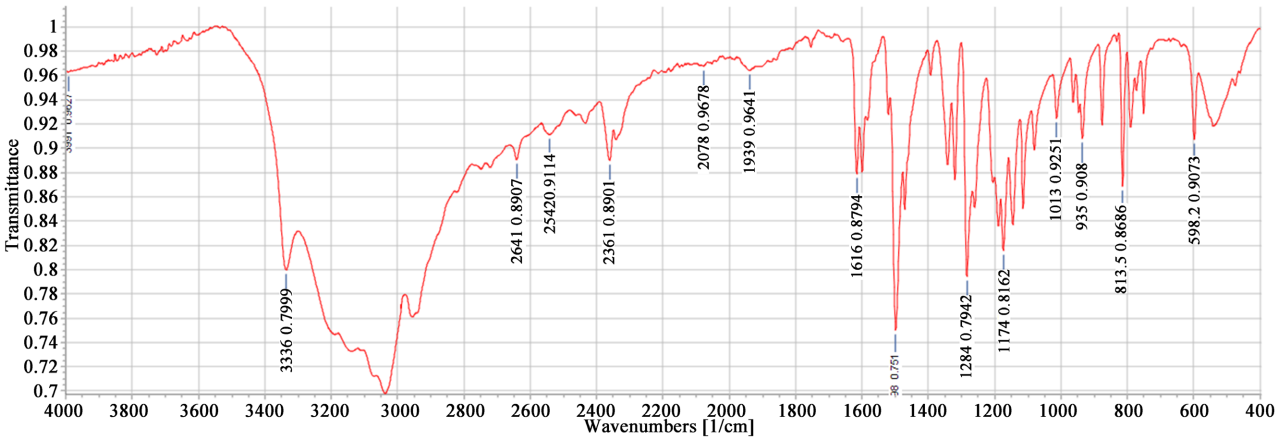


Figure 1. FT-IR spectrum of (*E*)-4-(2-((4-hydroxy-2*H*-chromen-2-ylidene)amino)ethyl)benzene-1, 2-diol (**1**).

3.3. Proton and Carbon-13 NMR Spectra

The proton and carbon-13 NMR spectra of **1** and **2** were recorded on Bruker DRX-500, −400, and −300 MHz instruments and calibrated on residual undeuterated solvent signals as an internal standard.

The ^{1}H NMR spectrum of **1** (Figure 3) revealed, in addition to the aromatic (7.55, 7.38, 6.96 ppm) and alkyl signals (4.67, 3.82 ppm), the presence of three

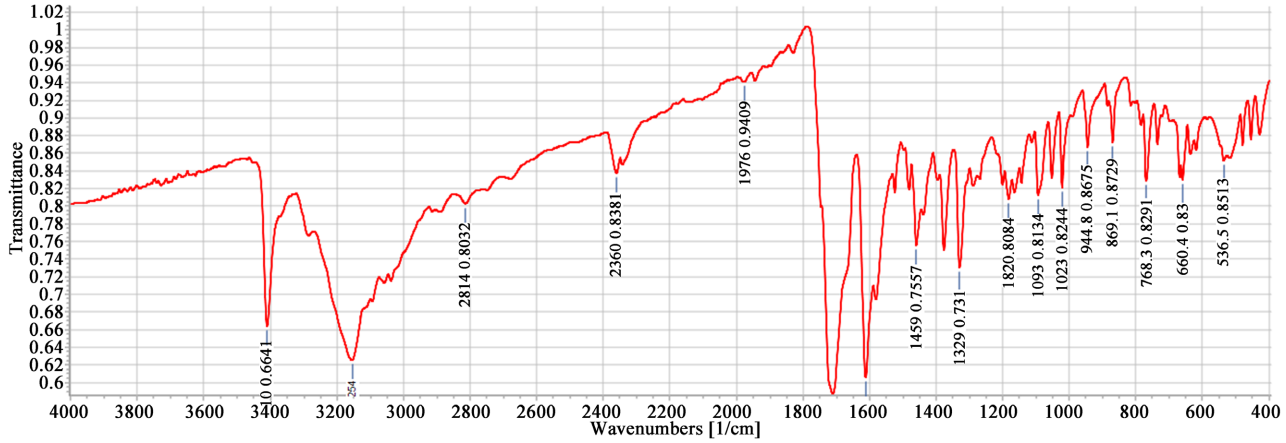


Figure 2. FT-IR spectrum of (*E*)-3-((3, 4-dihydroxyphenethyl) imino) indolin-2-one (**2**).

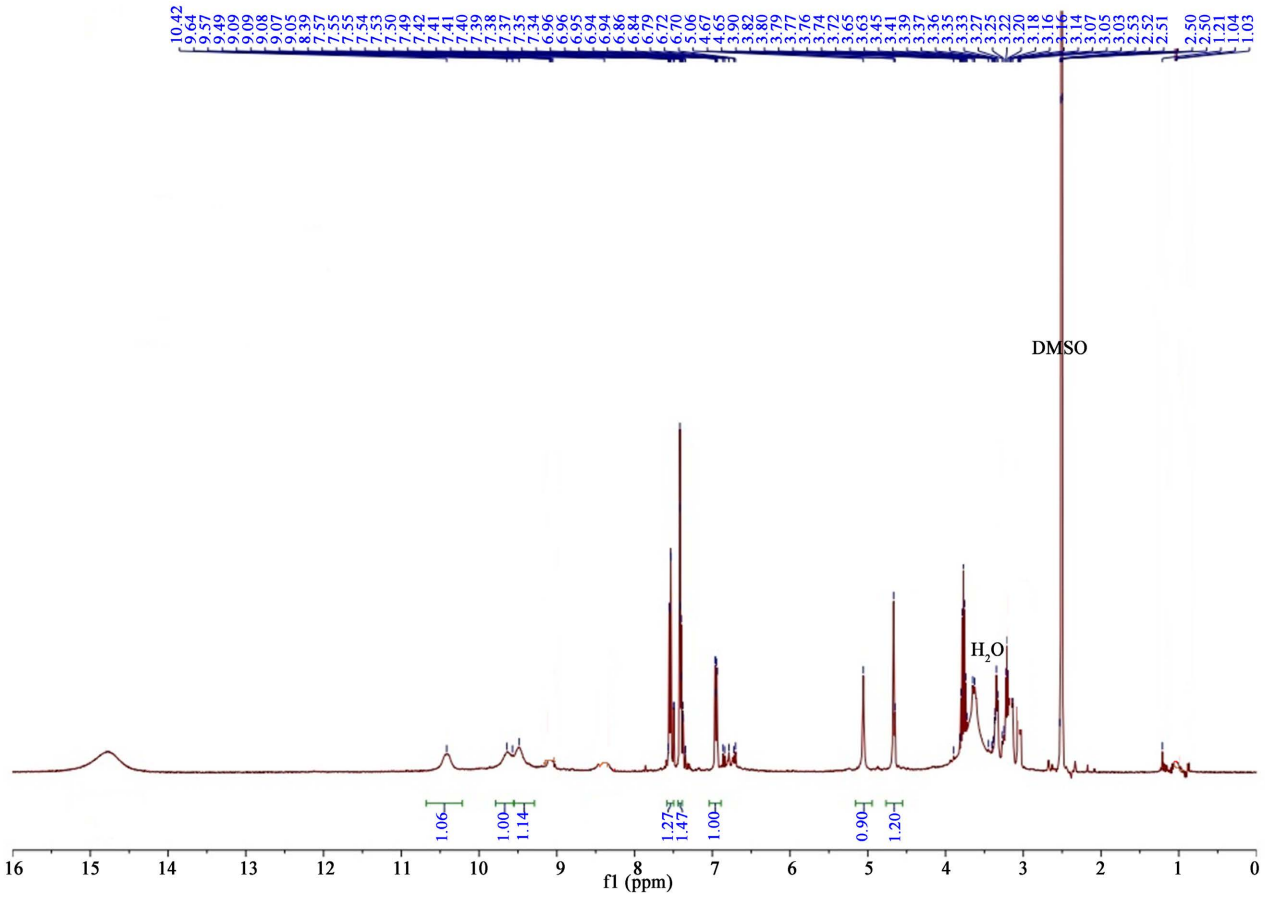


Figure 3. Proton NMR spectrum of **1**.

broad signals at δ 10.42, 9.64 and 9.49 ppm, assignable to the three hydroxyl protons. The ^{13}C NMR spectrum (Figure 4) displayed characteristic signals at δ 146.1, 152.7, 152.9 and 189.7 ppm, accounting for three carbons linked to the hydroxyl groups and the imine carbon respectively [24] [25].

The ^{1}H NMR spectrum of **2** (Figure 5) revealed, in addition to the expected aromatic (7.41, 6.94 ppm) and alkyl signals (4.74, 4.48 ppm), two broadened peaks at 10.37 and 9.62 ppm accounting for the two hydroxyl protons, while the signal at 8.27 ppm is assignable to the amide proton of the indolinone moiety. The ^{13}C NMR spectrum of **2** (Figure 6) displayed signals at 152.7, 154.1, 176.5 and 190.2 ppm assignable to two carbons linked to the hydroxyl groups, imine carbon and amide carboxyl carbon respectively [24] [25].

3.4. Powder X-Ray Diffraction Studies

Figure 7 and Figure 8 depict the powder pattern of all the synthesized Schiff bases. The degree of crystallinity of the synthesized Schiff bases was determined by obtaining their powder X-ray diffraction pattern. It should be noted that the powder pattern of (E)-4-(2-((4-hydroxy-2H-chromen-2-ylidene)amino)ethyl)benzene-1, 2-diol (**1**) Figure 7 indicates the porous nature of the molecule, which can be exploited for adsorption filtration studies [26].

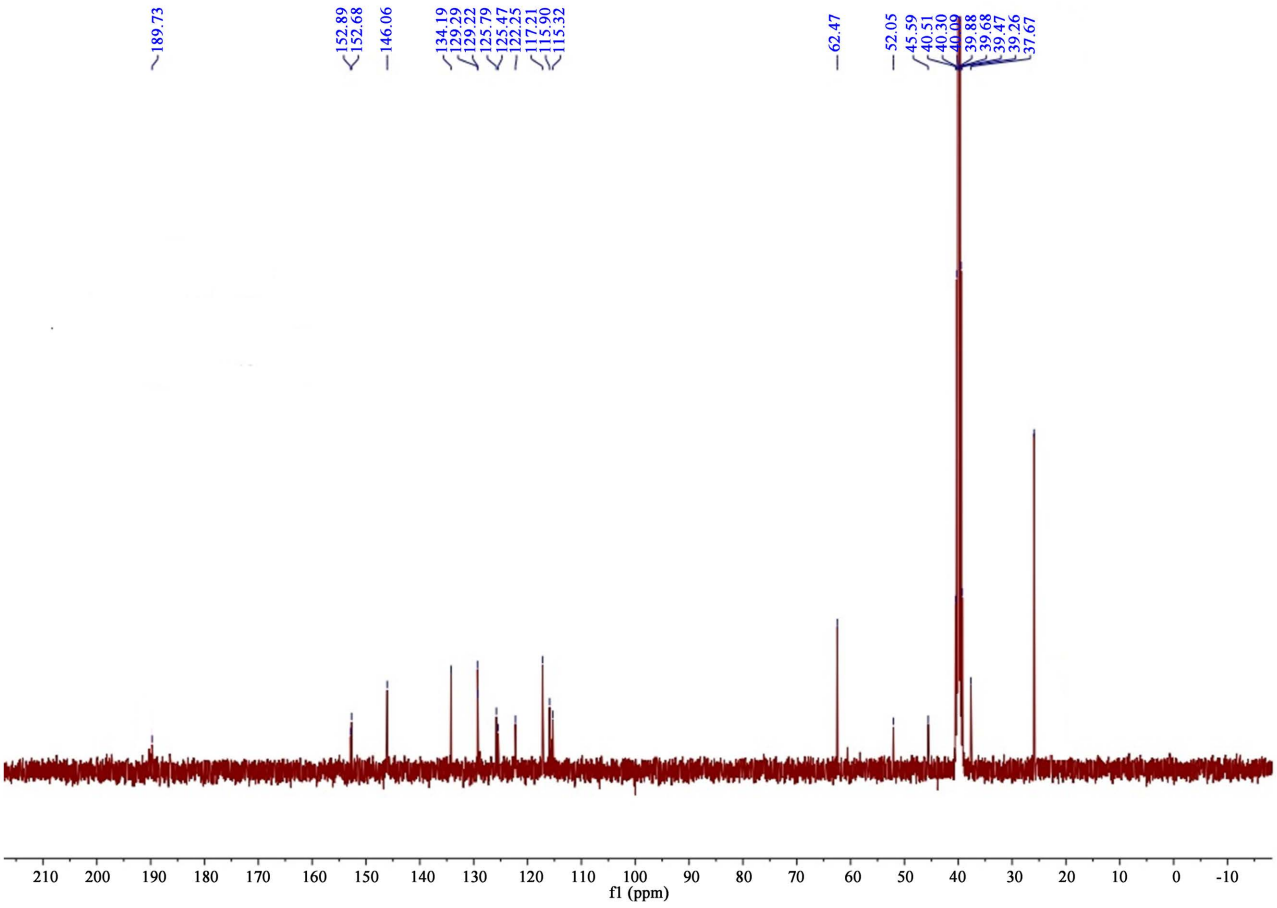


Figure 4. Carbon-13 NMR spectrum of **1**.

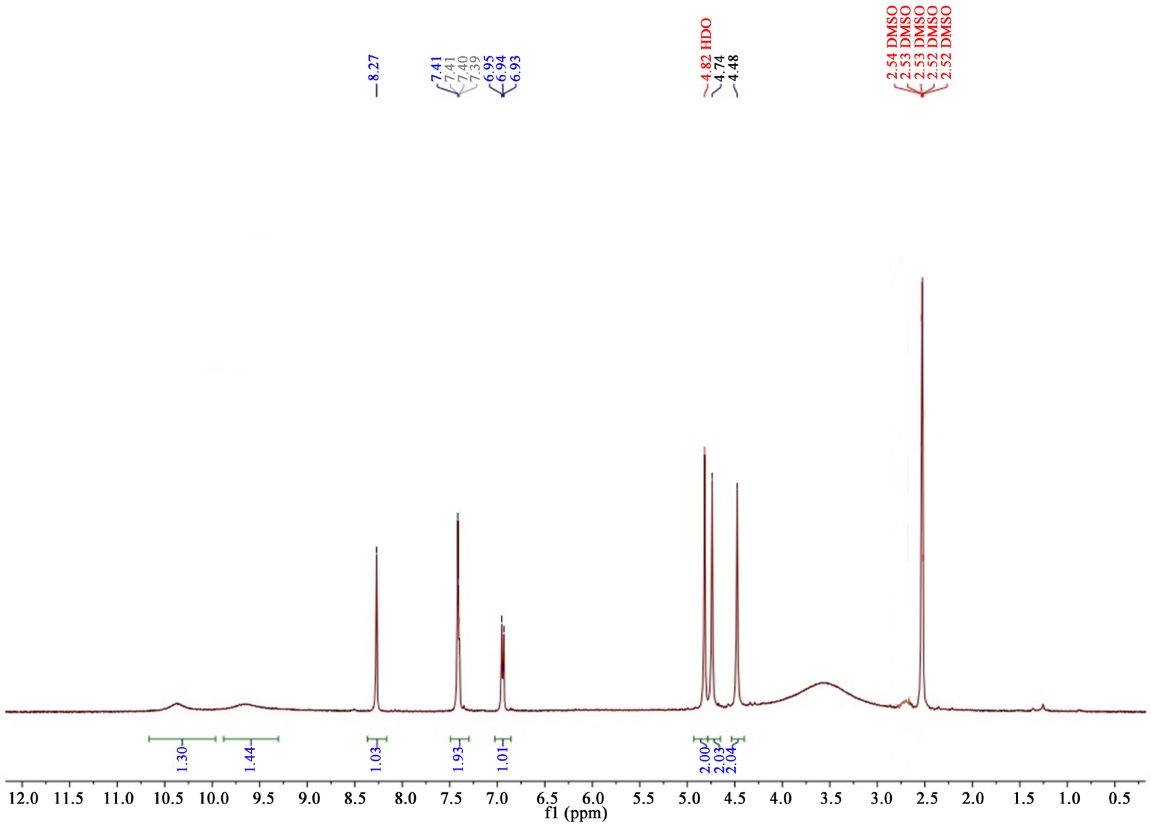


Figure 5. Proton NMR spectrum of **2**.

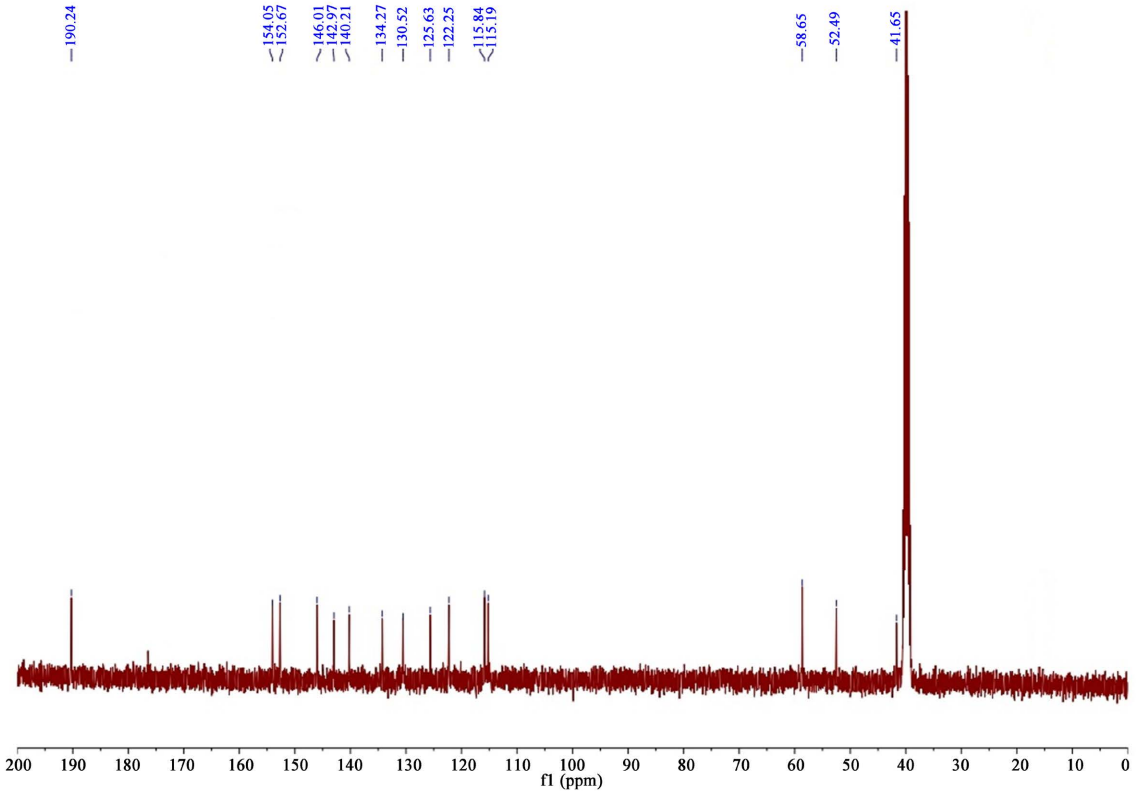


Figure 6. Carbon-13 NMR spectrum of **2**.

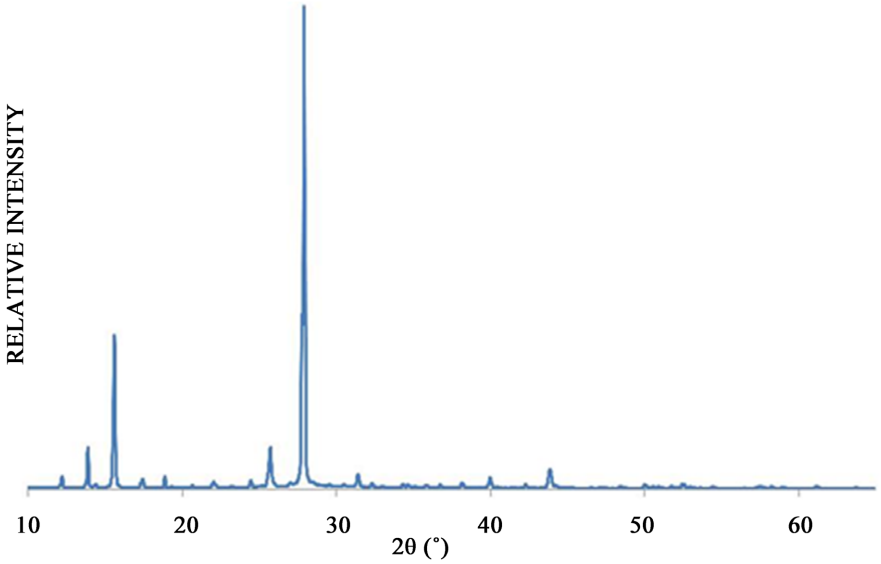


Figure 7. Powder X-ray diffractogram of **2**.

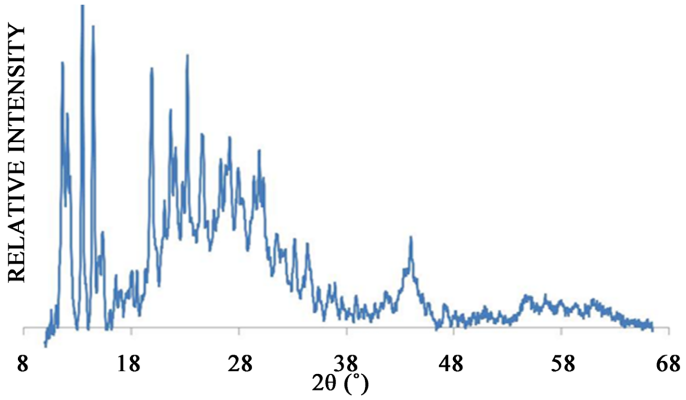


Figure 8. Powder X-ray diffractogram of **1**.

3.5. Computational Studies

Molecular modeling and quantum mechanical semi-empirical calculations were carried out using Spartan 14 program, so as to gain a better insight on the proposed molecular structures of the prepared compounds, since their single crystals could not be isolated. The correct stereochemistry was assured through the exploitation and modification of the molecular coordinates to attain reasonable low energy molecular geometries. The minimum steric energy which was determined severally resulted to global minimum energies of −388.57 and −235.21 kJ/mol for $C_{17}H_{15}NO_4$ (**1**) and $C_{16}H_{14}N_2O_3$ (**2**) respectively.

The optimized geometries of the **1** and **2** are presented in Figure 9 and Figure 10 with chemical function descriptors highlighting the relevant pharmacophores. These are zero values descriptors based on quantum calculations or derived from molecular fields interactions. These descriptors which are important for properties such as lipophilicity, hydrogen bonding, solubility and molecular size of compounds are very relevant in the understanding of structure-reactivity

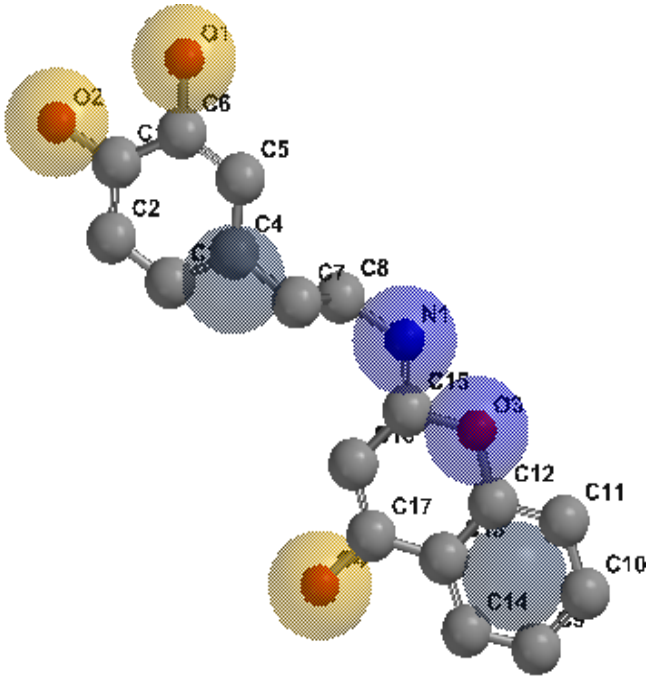


Figure 9. Optimized structure of **1** highlighting the chemical function descriptors.

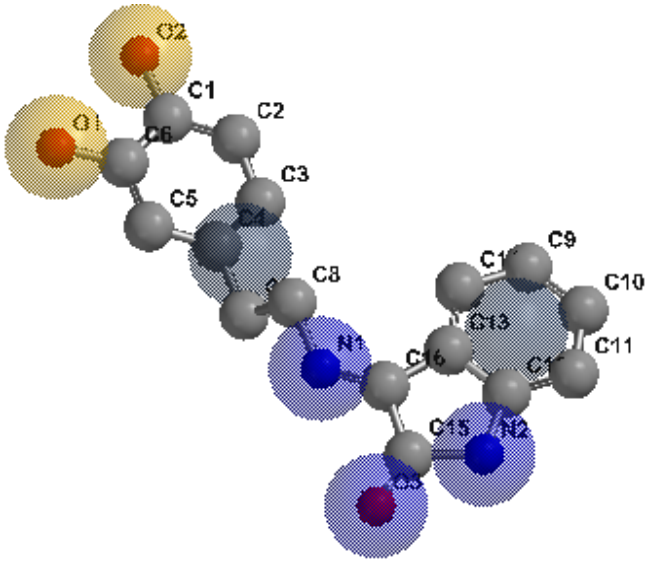


Figure 10. Optimized structure of **2** highlighting the chemical function descriptors.

relationships. The ligand-protein interactions of compounds can be inferred from these descriptors which have also been widely used to deploy accurate models for the predictions of toxicological and physicochemical properties of organic compounds [27].

For the optimized structure of $C_{17}H_{15}NO_4$ (**1**) the C-N bond lengths are within the range of 1.28 - 1.457 Å and the C-O bond lengths is 1.210 Å while for the structure of $C_{16}H_{14}N_2O_3$ (**2**) the C-N bond lengths falls within the range 1.296 - 1.461 Å which are all in line with previously reported results of similar compounds [28].

3.6. Antibacterial Activity

Four different bacterial strains used for the biological studies were two *Gram positive bacteria, Staphylococcus aureus*; *Bacillus subtilis* and two *Gram negative bacteria; Klebsiella pneumonia*, *Escherichia coli*. The efficiency of bacteria inhibition, determined by the broth dilution method, with the synthesized Schiff bases indicated that on an average, *E. coli* was the most inhibited with MIC values of 3.12 and 6.25 μg/mL, followed by *K. pneumonia* with MIC values of 6.25 μg/mL for both **1** and **2** as compared with the references standards with MIC values of 3.12 μg/mL. The MIC value of 3.12 μg/mL of **1** against *E. coli* indicates that it could be a better lead compound for further studies. Overall the Schiff base ligand $C_{17}H_{15}NO_4$ (**1**) exhibited greater activity compared to $C_{16}H_{14}N_2O_3$ (**2**) against all the bacterial strain used as presented in Table 1.

Table 1. *In vitro* antibacterial activity (MIC expressed in μg/ml).

Test sample	Sample concentration in μg/ml(MIC)			
	S. aureus	*B. subtilis*	*K. pneumonia*	*E. coli*
$C_{17}H_{15}NO_4$(**1**)	12.5	12.5	6.25	3.12
$C_{16}H_{14}N_2O_3$(**2**)	25.00	50.00	6.25	6.25
Ciprofloxacin	3.12	1.56	3.12	3.12
Norfloxacin	3.12	3.12	3.12	3.12

4. Conclusion

We have synthesized two dopamine derived Schiff base compounds using 4-hydroxycoumarin and isatin. The prepared compounds were characterized using solubility in different solvents, melting point determination, elemental analysis, FT-IR, ^{1}H- and ^{13}C NMR, and powder XRD spectroscopic techniques. The Schiff base **1** was found to inhibit *E. coli and K. pneumonia* with MIC values of 3.12 and 6.25 μg/mL, followed by *K. pneumonia*, compared to the reference standards with MIC values of 3.12 μg/mL, indicating that **1** could be a potential lead compound.

Acknowledgements

M.-L. L.W. and E. N. N. thank Professor You Song of the State Key Laboratory of Coordination Chemistry, Nanjing University in China for the spectral analyses.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Bozarth, M.A. (2017) Dopaminergic Pathways and Addiction. In: Wenzel, A.E., Ed.,

The Sage Encyclopedia of Abnormal and Clinical Psychology, Sage Publications, Thousand Oaks, 1178-1182.

[2] Grace, A.A. (2000) The Tonic/Phasic Model of Dopamine System Regulation and Its Implications for Understanding Alcohol and Psychostimulant Craving. *Addiction*, **95**, S119-S128.

[3] LaVoie, M.J., Ostaszewski, B.L., Weihofen, A., Schlossmacher, M.G. and Selkoe, D.J. (2005) Dopamine Covalently Modifies and Functionally Inactivates Parkin. *Nature Medicine*, **11**, 1214-1221. https://doi.org/10.1038/nm1314

[4] Khan, S.A., Asiri, A.M., Basheike, A.A. and Sharma, K. (2013) Green Synthesis of Novel Pyrazole Containing Schiff Base Derivatives as Antibacterial Agents on the Bases of *in- Vitro* and DFT. *European Journal of Chemistry*, **4**, 454-458. https://doi.org/10.5155/eurjchem.4.4.454-458.784

[5] Teuber, M. (2001) Veterinary Use and Antibiotic Resistance. *Current Opinion in Microbiolology*, **4**, 493-499. https://doi.org/10.1016/S1369-5274(00)00241-1

[6] da Silva C.M., da Silva D.L., Modolo L.V., Alves R.B., de Resende M.A., Martins C.V.B. and de Fátima Â. (2011) Schiff Bases: A Short Review of Their Antimicrobial Activities. *Journal of Advanced Research*, **2**, 1-8. https://doi.org/10.1016/j.jare.2010.05.004

[7] Mohini, Y., Prasad, R.B.N., Karuna, M.S.L., Kumar, C.G., Poornima, M. and Sujitha, P. (2013) Synthesis of Fatty Acid Schiff Base Esters as Potential Antimicrobial and Chemotherapeutic Agents. *Medicinal Chemistry Research*, **22**, 4360-4366. https://doi.org/10.1007/s00044-012-0450-y

[8] Shi, L., Ge, H.-M., Tan, S.-H., Li, H.-Q., Song, Y.-C., Zhu, H.-L. and Tan, R.-X. (2007) Synthesis and antimicrobial activities of Schiff bases derived from 5-chlorosalicylaldehyde. *European Journal of Medicinal Chemistry*, **42**, 558-564. https://doi.org/10.1016/j.ejmech.2006.11.010

[9] Cheng, L.-X., Tang, J.-J., Luo, H., Jin, X.-J., Dai, F., Yang, J., Qian, Y.-P., Li, X.-Z. and Zhou, B. (2010) Antioxidant and Antiproliferativeactivities of Hydroxylsubstituted Schiff Bases. *Bioorganic & Medicinal Chemistry Letters*, **20**, 2417-2420. https://doi.org/10.1016/j.bmcl.2010.03.039

[10] Bayeh, Y., Mohammed, F., Gebrezgiabher, M., Elemo, F., Getachew, M. and Thomas, M. (2020) Synthesis, Characterization and Antibacterial Activities of Polydentate Schiff Bases, Based on Salicylaldehyde. *Advances in Biological Chemistry*, **10**, 127-139. https://doi.org/10.4236/abc.2020.105010

[11] Toh-Boyo, G.M., Njong, R.N., Babette, E.M. and Nfor, E.N. (2021) Synthesis, Spectroscopic, Molecular Modeling and Anti-Fungal Studies of Some Divalent Metal Complexes of 4-Hydroxyacetophenone Isonicotinoyl Hydrazone. *Open Journal of Inorganic Chemistry*, **11**, 95-109. https://doi.org/10.4236/ojic.2021.113007

[12] Nfor, E.N., Husian, A., Majoumo-Mbe, F., Njah, I.N., Offiong, E.O. and Bourne, S.A. (2013) Synthesis, Crystal Structure and Antifungal Activity of Ni(II) Complex of a New Hydrazone Derived from Anti-Hypertensive Drug Hydralazine Hydrochloride. *Polyhedron,* **63**, 207-213. https://doi.org/10.1016/j.poly.2013.07.028

[13] Mikwa, C.C., Toh-Boyo, G.M., Njong, R.N., Ndosiri, B.N., Ndamyabera, C.A., Katsuumi, N., Mitani, Y., Nfor, E.N. and Akitsu, T. (2022) Bivalent Metal Complexes of a Novel Modified Nicotinic Acid Hydrazide Drug: Synthesis, Characterization and Anti-Tubercular Studies. *European Journal of Chemistry*, **13**, 63-68.

[14] Hehre, W.J. and Ohlinger, W.A. (2014) Spartan'14. Wavefunction, Inc, Irvine.

[15] Stewart, J.J.P. (1991) Optimization of Parameters for Semi-Empirical Methods. III Extension of PM3 to Be, Mg, Zn, Ga, Ge, As, Se, Cd, In, Sn, Sb, Te, Hg, Tl, Pb, and

Bi. *Journal of Computational Chemistry*, **12**, 320-341. https://doi.org/10.1002/jcc.540120306

[16] Goto, S., Jo, K., Kawakita, T., Mitsuhashi, S., Nishino, T., Ohsawa, N.and Tanami, H. (1981) Determination Method of Minimum Inhibitory Concentrations. *Chemotherapy*, **29**, 76-79.

[17] Winter, C.A., Risley, E.A. and Nuss, G.W. (1962) Carrageenin-Induced Edema in Hind Paw of the Rat as an Assay for Anti-Inflammatory Drugs. *Proceedings of the Society for Experimental Biology and Medicine*, **111**, 544-547.

[18] Majoumo-Mbe, F., Nfor, E.N., Sengeh, E.B., Njong, R.N. and Offiong E.O. (2015) Synthesis, Crystal Structure and Biological Activity of 1-(phthalazin-1(2H)-one) [(Pyridin-2-yl) ethylidene] Hydrazone and Its Cobalt (III) Complex. *Communications in Inorganic Synthesis*, **3**, 40-46.

[19] Nfor, E.N., Esemu, S.N., Ayimele, G.A., Eno, E.A., Iniama, G.E. and Offiong, E.O. (2011) Copper (II) and Nickel (II) Complexes of 4-Phenylsemicarbazones: Synthesis, Stereochemistry and Antimicrobial Activity. *Bulletin of the Chemical Society of Ethopia*, **25**, 361-370. https://doi.org/10.4314/bcse.v25i3.68668

[20] Sumrra, S.H., Ibrahim, M., Ambreen, S., Imran, M., Danish, M. and Rehmani, F.S. (2014) Synthesis, Spectral Characterization, and Biological Evaluation of Transition Metal Complexes of Bidentate N, O Donor Schiff Bases. *Bioinorganic Chemistry and Applications*, **2014**, Article ID: 812924. https://doi.org/10.1155/2014/812924

[21] Asiri, A.M. and Khan, S.A. (2010) Synthesis and Anti-Bacterial Activities of Some Novel Schiff Bases Derived from Aminophenazone. *Molecules*, **15**, 6850-6858. https://doi.org/10.3390/molecules15106850

[22] Nakamoto, K. (1978) Infrared and Raman Spectra of Inorganic and Coordination Compounds. Part B: Theory and Applications. John Wiley & Sons, Ltd., Hoboken, 156 p.

[23] Yong, J.N., Majoumo-Mbe, F., Samje, M. and Nfor, E.N. (2016) Synthesis, Molecular Structure and Anti-Onchocercal Studies of 1-(Phthalazin-1(2H)-one) [(Pyridin-2-yl) ethylidene] Hydrazone. *International Journal of Organic Chemistry*, **6**, 77-84. https://doi.org/10.4236/ijoc.2016.61008

[24] Silverstein, R.M., Webster, F.X. and Kiemle, D.J. (2005) Spectrometric Identification of Organic Compounds. 7th Edition, John Wiley & Sons, Inc., Hoboken.

[25] Pavia, D.L., Lampman, G.M. and Kriz, G.S. (2001) Introduction to Spectroscopy. Third Edition, Thomson Learning, Inc., Toronto, 579.

[26] Nfor, E.N., Burrows, A.D., Ndosiri, B.N., Keenan, L.L. and Offiong, E.O. (2019) Synthesis, Structure and Hydrogen Sorption Properties of a Pyrazine-Bridged Copper(I) Nitrate Metal-Organic Framework. *European Journal of Chemistry*, **10**, 195-200. https://doi.org/10.5155/eurjchem.10.3.195-200.1888

[27] Guha, R. and Willighagen, E. (2012) A Survey of Quantitative Descriptions of Molecular Structure. *Current Topics in Medicinal Chemistry*, **12**, 1946-1956. https://doi.org/10.2174/156802612804910278

[28] Nfor, E.N., Liu, W., Zuo, J.-L., You, X.-Z. and Offiong, E.O. (2006) Di-μ-acetato-bis[(2-acetylpyridinethiosemicarbazonato) Zinc (II)]. *Acta Crystallographica Section C*, **C62**, m211-m213. https://doi.org/10.1107/S0108270106009152