Indian Journal of Chemistry
Vol. 60B, August 2021, pp. 1110-1116

Designing a new vanillin Schiff base (Z)-4-((2-hydroxy-3-methoxy benzylidene)amino)-1,5-dimethyl-2-phenyl-1,2-dihydro-3*H*-pyrazol-3-one: Synthesis, characterization, crystal structure and biological studies

Gowri M*[a], Saranya B[a] & Athimoolam S[b]

[a] Department of Chemistry, Avinashilingam Institute for Home Science and Higher Education for Women, Coimbatore 641 043, India
[b] Department of Physics, University College of Engineering, Anna University Constituent College, Konam, Nagercoil 629 004, India

E-mail: sriadit.gowrisuresh@gmail.com; saranyabalakrishnan09@gmail.com; athi81s@yahoo.co.in

Received 30 August 2019; accepted (revised) 27 July 2021

Novel Schiff base containing antipyrine and *o*-vanillin has been synthesized and characterized by various physicochemical techniques such as FTIR, UV-Vis, CHN, ^{1}Hand ^{13}C NMR spectral studies. The thermal behavior of the title compound has been examined with Thermogravimetric-Differential thermal analysis (TG-DTA). The structural properties have been further examined by single crystal X-ray diffraction studies. The X-ray diffraction data shows that the compound contains four molecules in the asymmetric unit. Antifungal activity of the compound has been carried out for four different fungi *Aspergillus niger*, *Aspergillus flavus*, *Aspergillus terrus* and *Fusarium Sp* at three different concentrations, whereas the compound shows significant activity against the fungi *Aspergillus niger*.

Keywords: Schiff base, 4-amino antipyrine, *o*-vanillin, crystal structure, thermal analysis, antifungal activity

Chemists are very much focused on the Schiff base derived from nitrogen containing heterocyclic ring with carbonyl group as its important special center of attraction in many areas like biological, clinical, medicinal, analytical and pharmacological fields. Among them, 4-amino antipyrine based heterocyclic compounds have great importance as it is abundant in nature and have wide pharmacological activities[1-24]. 4-amino antipyrine is continued to attract considerable attention from theoretical points concerning the mode of binding and their general reactivity as a potential ligand[25-33]. Schiff bases of 4-amino antipyrine have an advantage as it has two potential donor sites and is likely to form three types of compounds with metal ions[34] viz., (i) chelates utilizing both donor atoms, (ii) amine salts, using only the amino nitrogen atom and (iii) two types of complexes, i.e., coordination only from the carbonyl oxygen or amine nitrogen atom. 4-amino antipyrine also has been used for the protection against oxidative stress as well as prophylactic of some diseases including cancer, and these are an important direction in medical applications.

The presence of a methoxy group adjacent to the phenolic hydroxyl gives a group of compounds isolated from plants called vanilloids, which includes substances such as vanillin, eugenol, and capsaicin[35]. Vanillin itself has its three isomeric forms such as vanillin, o-vanillin, iso-vanillin. Vanillin which is a main constituent of vanilla has some properties such as antioxidant, antimicrobial, anticarcinogenic, antimutagenic and free radical scavenging agents[36-54]. Vanillin, when administered orally, has no therapeutic effect because it undergoes rapid decomposition in the upper digestive tract. But vanillin, when combined with amino groups, form Schiff bases have a wide range of applications. The aldehyde group present in vanillin and the position of the substituent group determines the extent of its antifungal activity.

We aim to analyze all the previously determined characters of 4-amino antipyrine, and o-vanillin and to synthesize the Schiff bases from them. Thus, we were motivated to make an attempt to synthesize Schiff base and systematic study for the elucidation of the structure by various physicochemical techniques such as FTIR, UV-Visible, CHN, ^{1}H NMR, ^{13}C NMR spectroscopy. The analytical and physicochemical techniques confirm the structure of the resulting Schiff base. The structural properties were further examined by single crystal X-ray diffraction studies. The resulting Schiff base also screened for antifungal activity.

Experimental Section

Materials and methods

The melting point of the resulted Schiff base was determined with DIGITAL MELTING POINT APPARATUS using an open capillary tube with a heating rate of 10^{o}c/min. FTIR of the sample was recorded in the TENSOR 27 spectrometer. TG-DTA of the sample was recorded in Thermal Analyzer (SII, TG/DTA 6300), ^{1}H NMR(400MHz) and ^{13}C NMR (100MHz) spectra were recorded on a Bruker Advance (AC80) instrument in DMSO-d_6 using tetramethylsilane (TMS) as an internal standard. The chemical shift values were recorded in parts per million (ppm). The C, H, and N elemental analyses were performed using Thermal Finnigan Elemental Micro Analyzer. The synthesis of the Schiff base was monitored by TLC coated with silica gel.

Structural determination by single crystal X-ray diffraction studies

Single crystal structure data of the resulted Schiff base was collected using the X-ray with a wavelength of 0.71073Å, at room temperature with MoKα radiation using Bruker AXS KAPPA APEX-2 diffractometer equipped with graphite monochromator[55]. The structure was solved by direct methods and refined by full-matrix least-squares calculations using SHELXL-2014 [56]. All the H atoms are placed geometrically calculated bond distances, viz., -OH= 0.82Å, -CH = 0.93Å (for aromatic) and –CH =0.96Å (for – CH_3) constrained to ride on the concerned parent atom with U_{iso}. (H) = 1.2 or 1.5 U_{eq} (parent atom). The crystallographic data, details of data collection and the structure refinement are presented in Table I. The asymmetric part of the crystal structure consists of four units of the compound.

Antifungal studies

The compound was tested for antifungal activity against four representative fungal strains *Aspergillus niger*, *Aspergillus flavus*, *Aspergillus terrus and FusariumSp* at three different concentrations (10, 20, 30µl) by well diffusion method[57]. Fluconazole was used as a reference drug in terms of minimum inhibitory concentration (MIC).

Synthesis of (Z)-4-((2-hydroxy-3-methoxy benzylidene)amino)-1,5-dimethyl-2-phenyl-1,2-dihydro-3*H*-pyrazole-3-one Schiff base

Exactly 304mg (2mmole) of o-vanillin in 20ml of ethanol, added 406mg (2mmole) of 4-aminoantipyrine and refluxed over a water bath for about 3 hours.

Table I — Crystallographic parameters of the Schiff base

CCDC No.	1904666
Empirical formula	$C_{19}H_{19}N_3O_3$
Formula weight	337.37
Temperature	273(2) K
Wavelength	0.71073 Å
Crystal system	Triclinic
Space group	P -1
Unit cell dimensions	a = 14.4393(10) Å α = 89.9930(10)° b = 15.0796(10) Å β = 74.8090(10)° c = 16.6920(11) Å γ = 74.8780(10)°
Volume	3376.9(4) Å^3
Z	8
Density (calculated)	1.327 Mg/m^3
Absorption coefficient	0.092 mm^{-1}
F(000)	1424
Crystal size	0.24 × 0.19 × 0.16 mm^3
Theta range for data collection	1.267 to 25.00°.
Index ranges	-17 ≤ h ≤ 17, -17 ≤ k ≤ 17, -19 ≤ l ≤ 19
Reflections collected	33901
Independent reflections	11868 [R(int) = 0.0227]
Completeness to theta = 25.242°	97.30%
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	11868 / 0 / 917
Goodness-of-fit on F2	1.019
Final R indices [I>2sigma(I)]	R1 = 0.0395, wR2 = 0.1173
R indices (all data)	R1 = 0.0725, wR2 = 0.1535
Largest diff. peak and hole	0.249 and -0.194 e.Å^{-3}

The reaction is monitored by thin-layer chromatography. After the completion of the reaction, the resulting solution is kept aside without disturbing it. The Schiff base was separated as shiny yellow crystals. It was filtered, washed with petroleum ether and dried in vacuum: Yield 0.582g (86.40%). m.p. 210°C. CHN analysis % Obtained(Calculated):C 67.54(67.68), H 5.02(5.67), N 11.99(12.46); IR: 1658 cm^{-1}(C=N), 1747 cm^{-1}(C=O), 1150 (aliphatic C-O), 1200 cm^{-1}(Ar C-O), 3522 cm^{-1}(O-H), 1242 cm^{-1} and 1292 cm^{-1}(C-N); UV-Vis: 275nm (-C=N), 375nm (-OH); ^{1}H NMR (DMSO-d_6): 6.9-7.8 ppm (m, ArH), 2.4 ppm (s, N-CH_3), 3.17 ppm (s, C-CH_3), 3.7 ppm (s, O-CH_3), 9.9 ppm (s, CH=N), 13.89 (s, -OH); ^{13}C NMR(DMSO-d_6): 10.05, 35.50, 56.01 ppm (t, -CH_3), 76.62, 77.05, 77.47 ppm (t, $CDCl_3$), 148.03 to 150.36 (m, antipyrine ring moieties), 113.53 ppm to 134.25 ppm (m, ArC), 160.14 (C=O), 160.35 ppm (CH=N).

Results and Discussion

TG-DTA

The thermal stability of the resulted Schiff base was studied by simultaneous Thermo-Gravimetric and

Differential thermal analysis (TG-DTA) technique between 0-600°C at a heating rate of 2°C/min in the nitrogen atmosphere using Thermal Analyzer (SII, TG/DTA 6300). Figure 1 represents the thermal properties of Schiff base crystal carried out by TG-DTA. The DTA thermograph of the resulted Schiff base shows an endothermic peak at 208.3°C which can be attributed to the melting point of the compound and the compound is stable up to 274.4°C, and above this temperature, steady and gradual weight loss is noticed. Therefore it can be claimed that the title compound decomposes after melting. About 46% of the weight loss was noticed in between the temperature range 274°C and 309.6°C. Beyond the temperature 309.6°C, there is a slow decomposition of the compound up to 590°C leaving 53.2% as residue.

Based on the above spectral techniques like FTIR, UV- Visible, H^1NMR, C^{13}NMR and TG-DTA and CHN analysis, the structure of the compound is given in Figure 2.

Single crystal XRD studies

The compound was crystallized from a solvent evaporation solution growth technique. Block type single crystals suitable for X-ray diffraction were used for the X-ray diffraction studies. The crystallographic

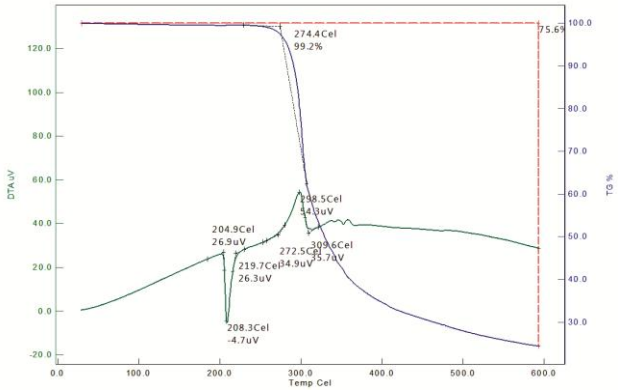

Figure 1 — TG-DTA spectrum of the Schiff base

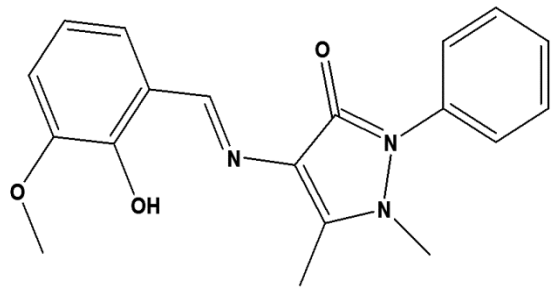

Figure 2 — The structure of the resultant Schiff base

data collection, using the X-ray with a wavelength of 0.71073Å, was collected at room temperature with MoKα radiation using Bruker AXS KAPPA APEX-2 diffractometer equipped with graphite monochromator[55].

The structure was solved by direct methods and refined by full-matrix least-squares calculations using SHELXL-2014[56]. All the H atoms are placed geometrically calculated bond distances, viz., -OH= 0.82Å, -CH = 0.93Å(for aromatic) and –CH =0.96Å (for $–CH_3$) constrained to ride on the concerned parent atom with U_{iso}. (H) = 1.2 or 1.5 U_{eq} (parent atom). The crystallographic data, details of data collection and the structure refinement are presented in Table I. The asymmetric part of the crystal structure consists of four units of the compound. The ORTEP view of the four asymmetric units of the crystal structure plotted at 50% probability thermal displacement ellipsoids with the atom numbering scheme are shown in Figure 3 (a), (b), (c), (d)[58].

Molecular Geometry and crystal packing

The compound crystallized with four molecules in the asymmetric part and eight molecules in the centrosymmetric triclinic unit cell. The phenyl and substituted phenyl rings are oriented with an average angle of 62.6°[55] to each other in all the molecules in the unit cell. Five membered rings are almost parallel between the molecules in the unit cell. The compound features classical and non-classical hydrogen bonds that stabilize the crystal structure. The non-covalent interactions are specially studied around the world for molecular conformations and other physicochemical properties. The classical O-H…N and non-classical C-H…O interactions lead to two self–associated S(6) motif. These self-associated motifs are formed through intramolecular interaction. The hydrogen bonding dimensions are listed in Table II and the packing arrangement of molecules is depicted in Figure 4. Further, the supramolecular assembly is achieved through ring $R_2^1(7)$ motifs in the lattice[59]. These motifs are alternately arranged and connected along the *b*-axis of the unit cell forming an infinite chain extending along the *b*-axis. These chain and ring motifs are stacked at z = 0 and 1 making the region as the hydrophilic region and the z = 1/2 is observed to hydrophobic region. This hydrophobic region is stabilized through C-H...π interactions. Alternate hydrophilic and hydrophobic layers are commonly occurring in many hydrogen bonded

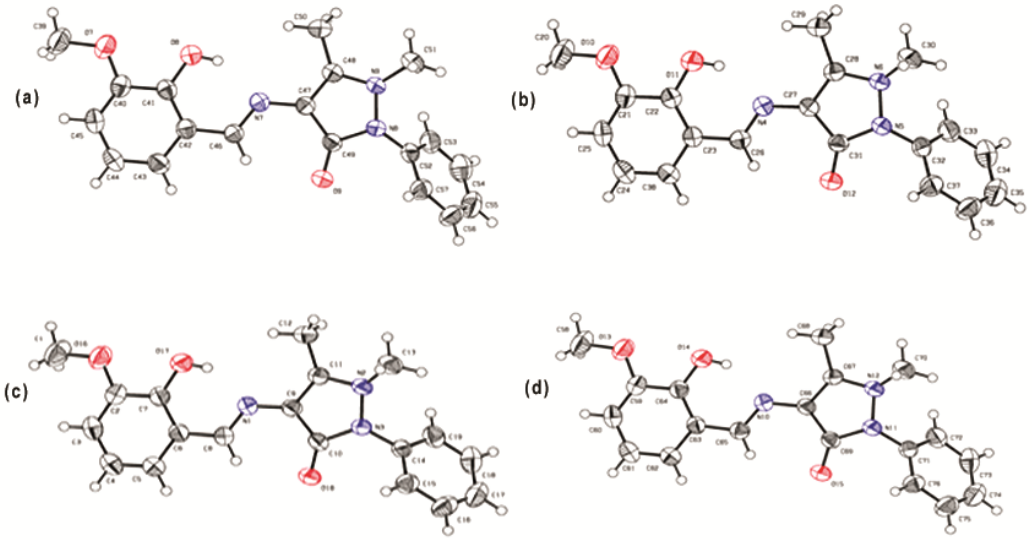

Figure 3 — a,b,c,dMolecular structures of the four asymmetric units present in the compound with 50% probability thermal displacement ellipsoids

Table II — Hydrogen bonding geometry in the Schiff base crystal

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
O(11)-H(11)...N(4)	0.82	1.86	2.585(3)	147
C(26)-H(26)...O(12)	0.93	2.4	3.057(3)	128
C(30)-H(30A)...O(18)#1	0.96	2.61	3.556(4)	167
C(29)-H(29A)...O(16)#2	0.96	2.66	3.464(4)	142
C(29)-H(29B)...O(18)#1	0.96	2.33	3.204(4)	151
O(17)-H(17)...N(1)	0.82	1.86	2.589(3)	147
C(8)-H(8)...O(18)	0.93	2.39	3.057(3)	128
C(12)-H(12A)...O(10)#2	0.96	2.53	3.457(4)	163
C(12)-H(12B)...O(12)	0.96	2.47	3.203(4)	133
C(13)-H(13A)...O(12)	0.96	2.61	3.554(4)	168
O(8)-H(8A)...N(7)	0.82	1.86	2.586(3)	147
C(46)-H(46)...O(9)	0.93	2.4	3.058(3)	128
C(51)-H(51A)...O(15)	0.96	2.61	3.553(4)	168
C(50)-H(50A)...O(13)#3	0.96	2.53	3.458(4)	164
C(50)-H(50B)...O(15)	0.96	2.48	3.202(4)	132
O(14)-H(14)...N(10)	0.82	1.86	2.585(3)	147
C(65)-H(65)...O(15)	0.93	2.4	3.057(3)	128
C(68)-H(68A)...O(7)#3	0.96	2.64	3.461(4)	144
C(68)-H(68B)...O(9)#1	0.96	2.34	3.203(3)	149
C(70)-H(70A)...O(9)#1	0.96	2.61	3.556(4)	168

Symmetry transformations used to generate equivalent atoms: #1 x,y+1,z #2 -x+2,-y+1,-z+1 #3 -x,-y+1,-z

molecular assemblies which are responding to many unique properties of the material.

Intermolecular interactions, especially classical and non-classical hydrogen bonds, are playing a crucial role in the formation of crystalline solids and their physicochemical properties. These hydrogen bonding interactions are useful in comparing the stability of molecular conformations and crystalline lattices between similar molecules[59]. The crystal packing is stabilized through classical O-H…O hydrogen bond, non-classical C-H...O, C-H…πhydrogen bonds, and π-π interactions. Interestingly, the classical O-H…O hydrogen bond connects the molecules along the *a*-axis of the unit cell in a zig-zag fashion in Figure 5.

Antifungal activity

The Antifungal activity of the Schiff base ligand was evaluated using the Well diffusion method. The fungal spores (*Aspergillus niger*, *Aspergillus flavus*, *Aspergillus terrus and Fusarium Sp*) were grown on

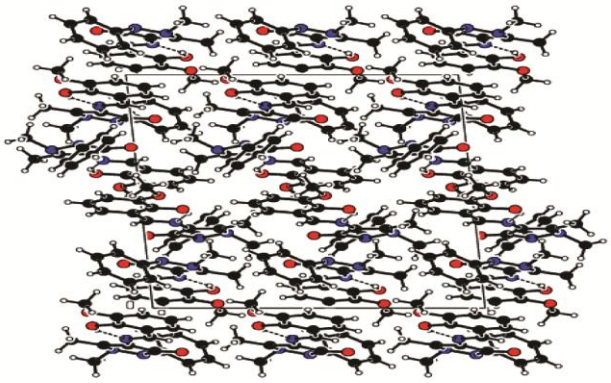

Figure 4 — Packing of the molecules in the triclinic unit cell is viewed down along *a*-axis. H-bonds are shown as dashed lines

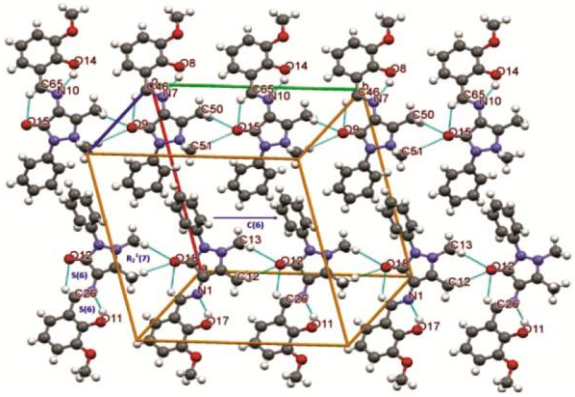

Figure 5 — O-H…O hydrogen bonds lead to chain C(11) motifs along the *a*-axis of the unit cell. H-bonds are shown as dashed lines

Table III — Antifungal activity of the Schiff base

Fungus	Zone of Inhibition (mm)				
	10 µL	20 µL	30 µL	Chloroform	Standard
A.niger	2	2	3	–	3
A.flavus	–	2	2	–	3
A.terreus	–	–	–	–	6
Fusarium Sp	–	2	2	–	4

potato dextrose broth (pH 5.0). The diluted fungal spores were (100µl) uniformly spread on Malt extract agar plate. After 2 to 3 minutes wells were made on the plate using a sterile cork borer (10mm). To the well 10µl to 30µl of the samples were added with negative control (chloroform) and the standard drug as a positive control (Fluconazole 10mg/ml). The plates were incubated at 30°C for 48hrs. The zone of inhibition was calculated and given in Table III.

Conclusion

The reported work is concerned with the synthesis, spectral characterization, crystal structure, and antifungal activity of the resulted Schiff base (Z)-4-((2-hydroxy-3-methoxy benzylidene)amino)-1,5-dimethyl-2-phenyl-1,2-dihydro-3*H*-pyrazole-3-one. The resulted compound crystallizes in the triclinic crystal system. The classical O-H…N, non-classical C-H…O interactions, and C-H…π interactions help to stabilize the crystal structure of the Schiff base. The antifungal activity of the Schiff base was screened with four representative fungal strains *Aspergillus niger*, *Aspergillus flavus*, *Aspergillus terrus and Fusarium Sp* at three different concentrations (10, 20, 30µl) and the *Aspergillus niger*is found to be a comparable activity like the standard drug Fluconazole at 30 µl.

Acknowledgments

The authors have gratefully acknowledged the financial support by University Grants Commission, New Delhi, sanctioned in the name of an in-house project by Avinashilingam Institute for Home Science and Higher Education for Women, Coimbatore, Tamil Nadu, India.

Supplementary Information

Supplementary information is available on the website http://nopr.niscair.res.in/handle/123456789/60.

CCDC 1904666 (Ref. 60) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via https://www.ccdc.cam.ac.uk/structures/ or by emailing data request@ccdc.cam.ac.uk or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 IEZ, UK, fax: +44(0)1223-336033.

References

1 Teng Y, Liu R, Yas S, Pan X, Zhang P & Wang M, *J Fluoresc*, 20(1) (2010) 381.URL: https://link.springer.com/journal/10895

2 Raman N, Jeyamurugan R, Sudharsan S, Karuppasamy & Mitu L, *Arab J Chem*, 6(2) (2013) 235. URL: https://www.journals.elsevier.com/arabian-journal-of-chemistry

3 Abdel Rahman A H, Ahmed A H A & Ramiz M M, *J Chem Het Comp* , 46(1) (2010) 72. URL: https://www.springer.com/chemistry/organic+chemistry/journal/10593

4 Santos M P, Antunes M M, Joao Noronha, Eduarda Femandes & Vieira J S C, *Euro J Med Chem*, 45 (2010) 2258. URL: https://www.journals.elsevier.com/european-journal-of-medicinal-chemistry

5 Raman N, Thangaraja C & Johnsonraja S, *CEJC*, 3(3) (2005) 537. URL: https://link.springer.com/journal/11532

6 Joseph J, Nagashri K & AyishaBibin Rani G, *J Sau Chem Soc*, 17 (2013) 285. URL: https://www.journals.elsevier.com/journal-of-saudi-chemical-society

7 Biju Bennie R, Theodore David S, Sivasakthi M, Asha Jeba Mary S, Seethalakshmi M, Daniel Abraham S, Joel C & R

Antony, Sythesis, *J Chem Sci Trans*, 3(3) (2014) 937. URL: http://www.e-journals.in
8 Anupama B, Padmaja M & Gyana Kumari C, *E-J Chem*, 9(1) (2012) 389. URL: https://www.eurjchem.com
9 Omar Hamad & Shihab Al-Obaidi, *J Bioinorg Chem App*, 6 (2012). URL: https://www.hindawi.com/journals/bca/
10 Foziah A Al-Saif, Int *J Elec chem Sci*, 8 (2013) 10424. URL: http://www.electrochemsci.org
11 Anupama B, Sunita M, Shiva Leela D, Ushaiah B & Gyana Kumari C, *J Fluoresc*, (2014). URL: https://link. springer.com/journal/10895
12 Raman N, Thalamuthu S, Dhaveethu Raja J, Neelakandan M A & Sharmila Banerajee, *J Chil Chem Soc*, 53 (2008). URL: https://www.jcchems.com
13 Mohanambal D & Arul Antony S, *Res J Chem Sci*, 4(7) (2014) 1. URL: http://www.isca.in/rjcs
14 Manjunath M, Ajaykumar D Kulkarni, Gangadhar B Bagihalli, Shridhar Malladi & Sangamesh A Patil, *J Mole Struc*, 1127 (2017) 314. URL: https://www.journals. elsevier.com/journal-of-molecular-structure
15 Kalanithi M, Rajarajan M & Tharmaraj P, *J Coord Chem*, 64(8) (2011) 1436. URL: https://www.tandfonline. com/ loi/gcoo20
16 Leelavathy C & Arulantony, *J Spec Acta Part A: Mol Biomol Spec*, (2013). URL: https://www.journals.elsevier. com/ spectrochimica-acta-part-a-molecular-and-biomolecular-spectroscopy.
17 Mostafa M Ghorab, Marwa G El-Gazzar & Mansour S Alsaid, *Int J Mol Sci*, 15 (2014) 7539-7553. URL: https://www.mdpi.com/journal/ijms
18 Suresh M S & Prakash V, *Int J phy sci*, 5(14) (2010) 2203. URL: https://academicjournals.org/journal/IJPS
19 Raman N,Sakthivel A & Pravin N, *J Spec Acta Part A: Mol Biomol Spec*, 125 (2014) 404. URL: https://www.journals. elsevier.com/spectrochimica-acta-part-a-molecular-and-biomolecular-spectroscopy
20 Selwin Joseyphus R, Shiju C, Joseph J, Justin Dhanaraj C & Arish D, *J Spec Acta Part A:Mol Biomol Spec*, 133 (2014) 149. URL:https://www.journals.elsevier.com/spectrochimica-acta-part-a-molecular-and-biomolecular-spectroscopy
21 Jeena Pearl A & Abbs Fen Reji T F, *J Chem Pharm Res*, 5(1) (2013) 115. URL: http://www.jocpr.com
22 Jeena Pearl A & Abbs Fen Reji T F, *Int J Adv Pharm Bio Chem*, 3(2) (2014). URL: http://oaji.net/journal-detail.html?number=844
23 Gopalakrishnan S & Joseph J, *J Micobio*, 37(2) (2009) 141. URL: https://www.springer.com/life+sciences/microbiology/ journal/12275
24 Manjula B, Arul Antony S & Arul Antony S, *Res J Chem Sci*, 3(12) (2013) 22. URL: http://www.isca.in/rjcs
25 Gowri M & Daniel Thangadurai T, *Mol Crys & Liq Crys*, 606 (2015) 199. URL: https://www.tandfonline. com/ loi/gmcl20
26 Ali P, Meshram J, Sheikh J, Tiwari V, Dongre R & Hadda T B, *J Med Chem Res*, 21 (2012) 157. URL: https://link. springer.com/journal/44
27 Rama N, Sobha S, Selvaganapathy M & Mahalakshmi R, *J Spec Acta Part A: Mol Biomol Spec*, 96 (2012) 698. URL:https://www.journals.elsevier.com/spectrochimica-acta-part-a-molecular-and-biomolecular-spectroscopy
28 Raman N & Sobha S, *J Inorg Chem Com*, 17 (2012) 120. URL: https://pubs.acs.org/journal/inocaj
29 Mosea Selvakumar P, Suresh E &Subramaian P S, *J Poly*, 26 (2007) 749. URL: https://onlinelibrary.wiley.com/ journal/10990518
30 Pin- xian Xi, Zhi-hong Xu, Xiao-hui Liu, Feng-juan Chen, Zheng-zhi Zeng, Xiao-wen Zhang & Ying Liu, *J Fluoresc*, 19 (2009) 63.URL: https://link.springer.com/journal/10895
31 Souza P, Machado P, Carvalho B, Binatti I, Krambrock K, Molphy Z, Kellett A, Elene C P & Priscila P S, *J Mol Struc*, (2018). URL: https://www.journals.elsevier.com/journal-of-molecular-structure
32 Layla A Mohammed, Afag J Kadhim & Nadia H Aubaid, *J Acta Chi Pharm Ind*, 3(2) (2013) 111. URL: https:// www.tsijournals.com/journals/acta-chimica-and-pharmaceutica-indica.html
33 Chandra S, Sharma A K & Sharma P, *J mole*, 14(1) (2009) 174. URL: https://www.mdpi.com/journal/molecules
34 Hossain M N, Alam J Begum, Akbar Ali M, Nazimuddin M, Smith F E & Hynes R C, *J Inorg Chi Acta*, 249 (1996) 207. URL: https://www.journals.elsevier.com/inorganica-chimica-acta
35 Beaudry F, Ross A, Lema P P & Vachon P, *J Phyt Res*, 24 (2010) 525. URL: https://onlinelibrary.wiley.com/journal/ 10991573
36 Jian-Ping Cheng, Qiu- Yue Lin, Rui-Ding Hu, Wen-Zhong Zhu, Hua-Qiong Li & Dong-Hang Wang, *CEJC*, 7(1) (2009) 105. URL: https://link.springer.com/journal/11532
37 Nagesh G Y, Mahadev U D & Mruthyunjayaswamy B H M, *J Pharm Sci Rev Res* , 31(1) (2015) 190. URL: http://www.globalresearchonline.net
38 Fugu M B, Ndahi N P, Paul B B & Mustapha A N, *J Chem Pharm Res*, 5(4) (2013) 22. URL: http://www.jocpr.com
39 Sirajuddin M, Ali S, Shah F, Ahmad M & Tahir M, *J Iran Chem Soc*, 11 (2014) 297. URL: https://link.springer. com/journal/13738
40 Sridevi C, *J Med Bioeng*, 4(5) (2015). URL: http:// www.jomb.org
41 Mohamed G G & Sharaby C M, *J Spec Acta Part A*, 66 (2007) 949. URL: https://www.journals.elsevier.com/ spectrochimica-acta-part-a-molecular-and-biomolecular-spectroscopy
42 Mei-Ju Niu, Zhen Li, Guo-Liang Chang, Xiang-Jin Kong, Min Hong & Qing-fu Zhang, *J PLOS ONE*, 10(6) (2015). URL: https://journals.plos.org/plosone/
43 Subha L, Balakrishnan C, Thalamuthu S & Neelakantan M A, *J Coor Chem*, (2015). URL: https://www.tandfonline. com/ loi/gcoo20
44 Rizwana B & Santha Lakshmi S, *Int J Chem Res*, 4(1) (2012) 464. URL: https://ijcr.info/index.php/journal
45 Sam N, Affan M A, Salam M A, Ahmad F B & Asaruddin M R, *J Inorg Chem*, 2 (2012) 22. URL: https:// pubs.acs.org/journal/inocaj
46 Tabassum S, Amir S, Arjmand F, Pettinari C, Marchetti F, Masciocchi N, Lupidi G & Pettinari R, *Euro J Med Chem*, 60 (2013) 216. URL: https://www.journals.elsevier.com/ european-journal-of-medicinal-chemistry
47 Tabassum S, Yadav S & Ahmad I, *J Org met Chem*, 752 (2014) 17. URL: https://www.journals.elsevier.com/journal-of-organometallic-chemistry
48 Yousef T A, Abu El-Reash G M, Al-Jahdali M & El-Bastawesy R El-Rakhawy, *J Mol Struc*, 1053 (2013) 15. URL: https://www.journals.elsevier.com/journal-of-molecular-structure

49 Subin Kumar K & Aravindakshan K K, *J PharmChem Bio Sci*, 5(3) (2017) 271. URL: https://www.jpcbs.info

50 Marton A, Kusz E, Kolozsi C, Tubak V, Zagotto G, Buzas K, Quintieri L & Vizler C, *J Antican Res*, 36 (2016) 5743. URL: http://ar.iiarjournals.org/

51 Faghih Z, Neshat A, Wojtezak A, Faghih Z, Mohammadi Z & Varestan S, *J Inorg Chi Acta*, (2017). URL: https://www.journals.elsevier.com/inorganica-chimica-acta

52 Joseph V A, Georrage J J, Pandya J H & Jadeja R N, *J Theo Comp Sci*, 2(4) (2015). URL: https://www.journals.elsevier.com/theoretical-computer-science

53 Anjaneya Vasavi G S S, Sreeramulu J, Subba Reddy G V & Sreenatha Sharma T, *J Glob Tren Pharm Sci*, 9(2) (2018) 5535. URL: https://www.jgtps.com

54 Jantaree P, Lirdprapamongkol K, Kaewsri W, Thongsornkleeb C, Choowongkomon K, Atjanasuppat K, Ruchirawat S & Svasti J, *J Agri Food Chem*, (2017). URL: https://pubs.acs.org/journal/jafcau

55 Bruker (2001). SAINT and SMART. Bruker AXS Inc., Madison, Wisconsin,USA.

56 George M. *Acta Cryst Sec C*, C17 (2015) 3. URL: https: // journals.iucr.org/c/

57 Zhang, *J Braz Chem Soc*, 25(1) (2014) 20. URL: http:// jbcs.sbq.org.br/

58 Spek L, *Acta Cryst Sec D*, D65 (2009) 148. URL: https:// journals.iucr.org/d/

59 Bernstein J, Davis E, Shimoni L & Chang N, *Ang Chem Int Ed Eng*, 34 (1995) 1555. URL: https://onlinelibrary.wiley.com/journal/15213773

60 Marutha Gowri, CCDC 1904666: 4-{[2-hydroxy-3-methoxyphenyl)methylidene]amino}-1,5-dimethyl-2-phenyl-1,2-dihydro-3*H*-pyrazol-3-one, Experimental Crystal Structure Determination, CSD Communications, (2019). URL: https://www.ccdc.cam.ac.uk/Community/csd-communications/