Original Article: Synthesis, Spectral and Biological Studies of DHA Schiff Bases

Shubham BhagwatraoBiradar |Dnyaneshwar VithalNarte |Rushikesh Pradip Kale |KalimoddinInayatsab Momin |MarotiSayabuSudewad |Kundan Chandramani Tayade |Dhananjay Gangadhar Palke*

Department of Chemistry, RajarshiShahuMahavidyalaya, (Autonomous) Latur (M. S.), India

Use yor device to scan and read the article online

Citation S.B Biradar, D.V. Narte, R.P. Kale, K.I. Momin, M.S. Sudewad, K.C. Tayade, D.G. Palke, **Synthesis, Spectral and Biological Studies of DHA Schiff Bases**.*J. Appl. Organomet. Chem.*,**2021**,*1*(1), 41-47. Link

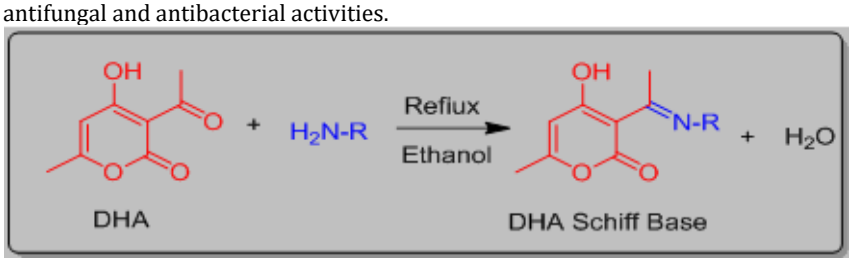
https://doi.org/10.22034/jaoc.2021.275758.1003

Article info:
Received: March 2, 2021
Accepted: April 7, 2021
Available Online: April 11, 2021
ID: JAOC-2103-1003
Checked for Plagiarism: Yes
Peer Reviewers Approved by:
Dr. SUNIL V. GAIKWAD
Editor who Approved Publication:
Professor Dr. Abdelkader Zarrouk

Keywords:
Dehydroacetic acid, Schiff Bases, Spectral and Biological study.

ABSTRACT

A new series of Schiff bases derived from DHA (Dehydroacetic acid) and aromatic primary amines were synthesized and characterized by elemental and spectral (Electronic, IR and ^{1}HNMR) analysis. The signals of ^{1}HNMR spectrum and characteristic peaks in IR spectra are used for the molecular structure elucidation of synthesized Schiff bases. The antimicrobial activities of synthesized compounds have been screened *in vitro* against *Escherichia coli*, *Staphylococcus aureus*, *Bacillus subtilis* bacterial species, *Candida albicans*and *Aspergillus niger*fungal organismand found to exhibit strong antifungal activity than antibacterial activity. Among the studied DHA Schiff base of 2-amino-4, 6-dimethylpyrimidine depicted discerning antifungal and antibacterial activities.



Introduction

Schiff bases are most widely used chelating agents in co-ordination chemistry [1-3]. Antiviral agents are very effective against mouse hepatitis virus (MHV) [4, 5]. Schiff bases and their complexes have broad range of application synthesized from the condensation of an amine scaffold with carbonyl compounds. The Schiff bases and their compounds exhibit a broad range of biological activities as

Corresponding Author:Dhananjay Gangadhar Palke (dhananjaypalke@gmail.com)*

antiproliferative, including antifungal, antibacterial, antimalarial, anti-inflammatory, antiviral, and antipyretic properties. Many Schiff bases are metal complexes and exhibit catalytic property, which play a significant role in the organic transformation to increase the yield of the product as well chemoselectivity of the reaction.[6]. Research studies have been done on synthesis of various Schiff bases derivatives from the reaction of dehydroacetic acid (DHA) and aliphatic/aromatic primary amines, hydrazides, and thiosemicarbazides [7-8].Spectral studies of Schiff bases containing heterocyclic ring are comparatively minor[9-10].

Based on what stated above and to pursue our research on the synthesis of novel DHA-Schiff and their biological properties, herein we have reported the synthesis, characterisation and biological activity of novel DHA- Schiff derivativres.

Experimental

DHA was purchased from E-Merck Germany, 4-amino phenol, 2-aminopyridine, 2-amino-6-nitrobenzothiazole, 2-amino-5-chlorobenzophenone and 2-amino-4,6-dimethylpyrimidine were obtained from Avra and Acros Organics chemicals. The solvents were dried and distilled before use as per reported procedure [11]. Elemental (C, H and N) analysis was carried out on Perkin Elmer CHN Analyser (2400). The electronic spectra were recorded on Shimadzu UV–VIS Spectrophotometer UV1700, in the range of 200–500 nm at our research center. The IR spectra of Schiff's bases were recorded on Perkin Elmer (1430) FTIR spectrophotometer in the range 4000 to 666 cm^{-1} by KBr pellet method and on alpha Brucker at our research centre RajarshiShahuMahavidyalaya (Autonomous) Latur. ^{1}HNMR spectra were recorded on Brucker FT 300/400/500 MHz NMR spectrophotometer in $CDCl_3$ solvent using TMS as reference. The biological activities (antibacterial and antifungal) of synthesized Schiff bases were tested against *Escherichia coli (E.coli)* (ATCC2331), *Staphylococcus aureus* (*S.aureus*) (NCIM-2079) and *Bacillus subtilis* (*B.subtilis*) (NCIM-2063) as bacterial strains and *Candida albicans* (*C.albicans*) (MTCC-227) and *Aspergillus niger (A.niger)* (NCIM-545) as fungal strains as per the procedure [12, 14] from our Biotechnology Research Centre.

Synthesis of schiffbases

DHA Schiff bases were synthesized by the addition of ethanolic solution of individual primary amine (0.05 mol) into hot ethanolic solution of DHA (Dehydroacetic acid) (0.05 mol) as per the procedure [13, 14] [**Figure 1].**

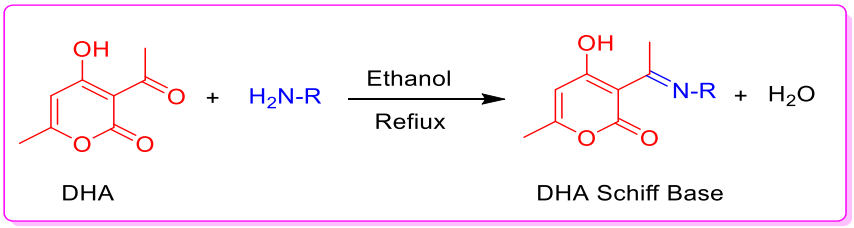
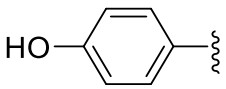
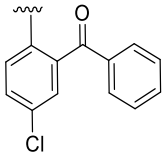
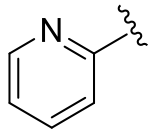
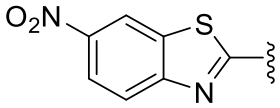
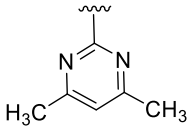


Figure 1. Synthesis of DHA Schiff bases

Entries	R	Entries	R
L_1		L_4	

L_2 

L_3 

L_5 

Results and Discussion

Elemental analysis

All the synthesized DHA Schiff bases are yellow, orange to brown coloured solids, stable to air and non-hygroscopic. They are insoluble in water and soluble in hot ethanol. Their physical characteristics and elemental analysis data are summarized in **Table 1.**

Table1. Elemental analysis

Entries	Compound Formula	Colour	F.Wt.	M.P. ^{0}C	Found/(Calculated) % C	H	N
L_1	$C_{14}H_{13}NO4$	Gray	259	120	63.92(64.86)	5.12(5.01)	5.34(5.40)
L_2	$C_{13}H_{12}N_2O_3$	Dark Orange	244	90	64.01(63.93)	04.64(4.92)	11.41 (11.47)
L_3	$C_{15}H_{11}N_3O_5S$	Orange	345	158	51.91(52.17)	3.24(3.18)	11.35(12.17) S 7.87(9.27
L_4	$C_{21}H_{16}NO_4Cl$	Yellow	379.5	98	64.54(66.40)	4.25(4.21)	3.72(3.68) Cl-8.55(9,35)
L_5	$C_{14}H_{13}N_3O_3$	Brown	271	85	62.25(61.99)	4.30(4.80)	14.69(15.50)

Spectral characterization

Electronic spectra

All the synthesized DHA Schiff bases exhibited weak absorption bands λ_{max} in the region 45871 to 42918 cm^{-1}, which was assigned to conjugated azomethine $\pi\rightarrow\pi^*$ transition appear for >C=N.

The absorption band λ_{max} in the region 40000 - 37453 cm^{-1} appeared due to $\pi\rightarrow\pi^*$and $n\rightarrow\pi^*$ transitions of >C=N in a heterocyclic ring of amine moiety i.e pyridine at 38785 cm^{-1}, thiazole 38934 cm^{-1} and Pyrimidine at 38979 cm^{-1}. Benzene ring also showed absorption at 40000 cm^{-1} [15].

All the DHA Schiff bases showed one more absorption band λ_{max} in the region 33167 to 31655 cm^{-1} assigned to lactone carbonyl group >C=O, auxochrome –OH attached to homoannular conjugated diene, which was closer to calculated value 31948 cm^{-1} [16].

Conjugated Lactone displayed absorption in the region of 50000-41666 cm^{-1}. The extended conjugation and auxochrome produce a bathochromic shift [15].

FTIR analysis

The absorption peak pattern in IR spectra exhibited complex nature due to various vibrational modes. However, with few objectives, only characteristic peaks which were specific to all Schiff bases related to enolic O-H, aromatic C=C, azomethine >C=N, aryl azomethine, lactone carbonyl C=O and enolic C-O/C=O of Schiff bases were taken into consideration for characterization.

In all the synthesized DHA Schiff bases the characteristic O-H stretching frequencies were observed as broad weak band at 3454 to 3368

cm^{-1} due to strong intermolecular hydrogen bonding between enolic O-H and N of azomethine group.

Azomethine >C=N stretching frequency is dependent on its substituent and mostly causes resonance interaction and H-bonding. In the present work azomethine (>C=N-) depicted strong absorption stretching vibration band in the region 1644-1634 cm^{-1}.

The peak in the region 1708 to 1685 cm^{-1} appeared due to>C=O lactone carbonyl stretching vibrations; peak in the region 1388 to 1333 cm^{-1}appeared due toaryl/aliphatic (C-N) stretching vibrations and the peak in the region 1256 to 1214 cm^{-1}appeared due to (C-O) enolic stretching vibrations.[15,16,17] IRCharacteristic IR frequencies are summarized in **Table 2.**

Table 2. Characteristic IR frequencies (cm^{-1}) of Schiff bases

Compounds	(O—H)	(>C=O)	(>C=N)	(>C=C<)	(C--N)	(C--O)
$L_1C_{14}H_{13}NO_4$	3427	1689	1646	1571	1358	1256
$L_2C_{13}H_{12}N_2O_3$	3419	1688	1644	1588	1333	1214
$L_3C_{15}H_{11}N_3O_5S$	3454	1691	1643	1564	1376	1234
$L_4C_{21}H_{16}NO_4Cl$	3368	1690	1641	1563	1382	1261
$L_5C_{14}H_{13}N3O_3$	3417	1708	1634	1590	1353	1216

^{1}HNMR Spectra

^{1}HNMR spectra of all the compounds were recorded in $CDCl_3$ at room temperature. The following signals, chemical shift value δ (ppm) relative to TMS as internal standard were observed:

Singlet signal at *δ* value 2.1—2.28 for the methyl group at C_6, singlet signal at *δ* value 14.72 —16.00 of enolic O-H group which is highly deshielded, singlet signal at *δ* value 5.00—5.94 belonging to H atom at C_5 and singlet signal at *δ* value 2.57—2.75 for the methyl group attached to azomethine C atom of DHA moiety and different signals of amine moiety.[17]

L_1 =^{1}HNMR (500 MHz, $CDCl_3$, *δ*, ppm : 2.26 (3H, s, C_6–CH_3), 15.88 (1H, s, O –H), 5.92 (1H, s, C_5–H), 2.58 (3H, s, N=C-CH_3,H bonded to 'C' azomethine) for DHA moiety,7.4 (2H, d, Ar–H), 7.6 (2H, d, Ar–H), 9.6 (1H, s, Broad) for phenol moiety.

L_2 = ^{1}HNMR (400 MHz $CDCl_3$, *δ*, ppm: 2.2 (3H, s, C_6–CH_3), 16.00 (1H, s, O –H), 5.8(1H, s, C_5–H), 2.6(3H, s, N=C-CH_3, H bonded to 'C' azomethine) for DHA moiety, 7.7-8.5 (4H, m, Ar) for pyridine moiety.

L_3 = ^{1}HNMR (400 MHz $CDCl_3$, *δ*, ppm: 2.1(3H, s, C6 –CH_3), 15.85(1H, s, O–H), 5.9(1H, s, C5 –H), 2.6(3H, s, N=C-CH_3, H bonded to 'C' azomethine) for DHA moiety, 7.7 (1H, m, C_5-H), 6.9-7.2 (2H, d, C_7& C_8-H), for benzothiazole moiety.

L_4= ^{1}HNMR (300 MHz $CDCl_3$, *δ*, ppm: 2.2 (3H, s, C_6 –CH_3), 15.54 (1H, s, O–H), 5.75(1H, s, C_5–H), 2.7(3H, s, N=C-CH_3,H bonded to 'C' azomethine) for DHA moiety, 2.3(3H, s, ring –CH_3), 7.4 -7.6 (5H, s, Ar.) 7.6 -7.8 (3H, m, Ar.) for benzophenone moiety.

L_5=^{1}HNMR (300 MHz $CDCl_3$, *δ*, ppm: 2.11 (3H, s, C_6–CH_3), 14.82(1H, s, O–H), 5.7(1H, s, C_5–H), 2.75(3H, s, N=C-CH_3, H bonded to 'C' azomethine) for DHA moiety, 2.34 (6H, s, two CH_3 to Ar), 7.6 (1H, s,), for pyrimidine moiety.

Screening for bioactivity

In vitro antibacterial and antifungal activities of the compounds were screened by considering zone of inhibition of growth. The synthesized DHA Schiff bases were screened with their

different concentrations with standard antibiotics such as streptomycin (1 mg/mL) and griseofulvin (1 mg/mL).

The DHA Schiff bases have shown harmonious antibacterial and antifungal action. All the DHA Schiff bases were found to be biologically active against *E.coli* with maximum zone of inhibition 21 mm by L_5. L_1, L_2 and L_3 showed moderate zone of inhibition 17 to 18 mm and L_4 has showed minimum zone of inhibition 15 mm against*E.coli.* L_5 showed 16.4 mm, maximum zone of inhibition against *S. aureus*. L_2 and L_4, were found to be moderate in growth inhibition while L_3 showed low activity with maximum zone of inhibition 9.00 mm against the same species. All the compounds were found to be moderate in growth with 11.3 mm zone of inhibition by L_2 while Schiff base L_4 low activity with 4.5 mm zone against *B. subtilis*. All the DHA Schiff bases have shown harmonious antifungal action. All compounds showed about 13 to 16 mm zone of inhibition and L_5 depicted maximum zone of inhibition 19 mm against *A. niger*. All compounds showed about 13 to 16 mm zone of inhibition, while L_2 showed 21 mm maximum zone of inhibition, along with the compound L_1 low zone of inhibition with 11.3 mm against human opportunistic pathogen, *C. albicans*. The bioactivity data is summarized in Table 3.

Table 3. Summarized bioactivity data

Sr. No	Compound	Antibacterial (mm) Zone of Inhibition			Antifungal (mm) Zone of Inhibition	
		B1	B2	B3	F1	F2
1	**L_1**	17.0	10.0	10.0	13.0	11.3
2	**L_2**	18.0	12.7	11.3	16.5	21.0
3	**L_3**	17.5	09.0	08.2	16.0	13.0
4	**L_4**	15.5	10.3	04.5	13.4	17.0
5	**L_5**	21.0	16.4	09.0	19.0	16.0
6	Streptomycin	28.5	19.5	16.0	00.0	00.0
7	Griseofulvin	00.0	00.0	00.0	22.0	25.0

B1 - *E. coli,* B2 -*S. aureus*, B3- *B. subtilis,* F1-*C. albicans*, F2- *A. niger*, NA-Not applicable

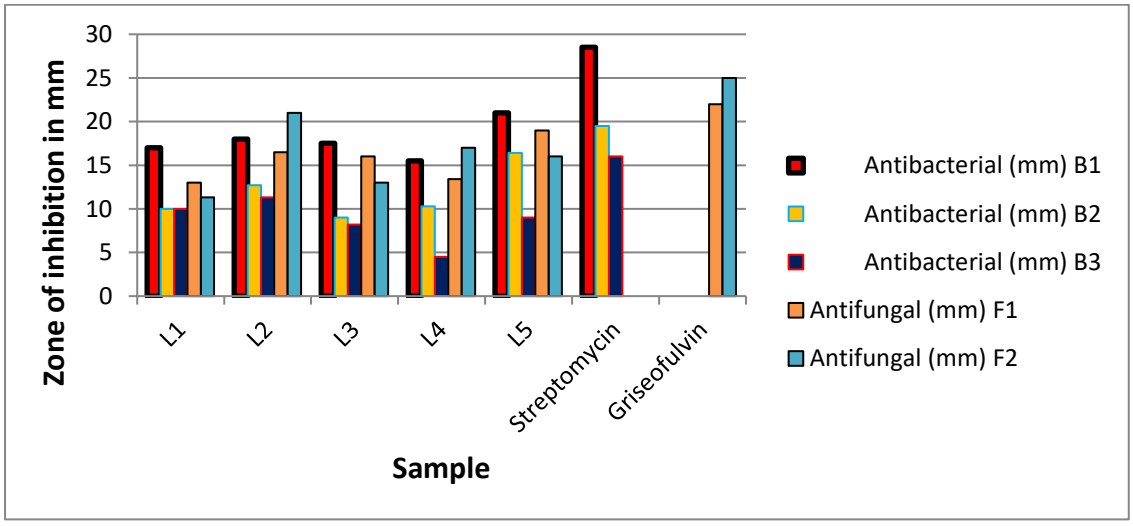


Figure 2. Graphical presentation of bioactivity

Conclusion

All the Schiff bases are yellow, orange to brown coloured solids, stable to air and non-hygroscopic. The composition of all synthesized Schiff bases was confirmed by elemental analysis and their structures were determined by IR and ^{1}HNMR spectroscopic techniques.All

the synthesized Schiff bases were found to possess strong antifungal activity than antibacterial activity. The compound L_5 the Schiff Base of 2-amino-4,6-dimethylpyrimidine exhibited the stronger inhibitor of growthas compared to other Schiff bases. Least growth inhibitory activity was shown by compound $L_4$the Schiff Bases of 2-amino-5-chlorobenzophenone.

Acknoledgement

The authors express sincere thanks to Principal RajarshiShahuMahavidyalaya, (Autonomous) Latur. Director Department of Chemistry, S. R. T. M. University, Nanded. Head, Department of Chemistry and Analytical Chemistry and All the staff of Department of Chemistry and Analytical Chemistry RajarshiShahuMahavidyalaya, (Autonomous) Latur. The authors are also thankful to A. A. Yadav IQAC Coordinator, S. H. Kathawate Savitribai Phule Pune University, Pune, Manisha Dhotre, S.S. Kulkarni Department of Biotechnology, RajarshiShahuMahavidyalaya, (Autonomous) Latur.

Orcid:

Shubham Bhagwatrao Biradar: *https://orcid.org/0000-0003-4270-4738*
DnyaneshwarVithalNarte: *https://orcid.org/0000-0001-5458-1945*
Rushikesh Pradip Kale: *https://orcid.org/0000-0002-7133-4820*
KalimoddinInayatsabMomin : *https://orcid.org/0000-0001-6297-6509*
MarotiSayabuSudewad: https://orcid.org/0000-0001-5303-7841
Kundan Chandramani Tayade: *https://orcid.org/0000-0001-5492-2121*
Dhananjay Gangadhar Palke: *https://orcid.org/0000-0002-3096-7269*

References

[1] S. Kannan, R. Remesh, *Polyhedron*,**2006**, *25*, 3095-3103.**[crossref], [Google scholar], [Publisher]**
[2] P.S. Mane, S.M. Salunke, B.S. More and T.K. Chondhekar; *Asian J. Chem*., **2012,***24*, 5, 2235-2238.**[Pdf], [Google scholar], [Publisher],**
[3] M.S. Karthikeyan, D.J. Prasad, B. Poojary, K.S. Bhat, B.S. Holla, N.S. Kumar, *Bioorg. Med. Chem.*, **2006**, *14*,7482-7489.**[crossref], [Google scholar], [Publisher]**
[4] D. Sriram, P.Yogeeswari, N.S.Myneedu, V. Saraswat, *Bioorg. Med. Chem. Lett.*,**2006,** *16*, 2127-2129.**[crossref], [Google scholar], [Publisher]**
[5] M. Ahmed, A. Dief, I.M.A. Mohamed, *J. BasicAppl.*,**2015,** *4*, 119-133. .**[crossref], [Google scholar], [Publisher]**
[6] a)D.A. Evans, J.M Janey, N. Magomedov, J.S. Tedrow, *Angew Chem. Int.Ed.*, **2001**, *40*, 1884.**[crossref], [Google scholar], [Publisher]**
b) S.V. Gaikwad, M. V. Gaikwad, P. D. Lokhande, J. Appl. Organomet. Chem., **2021**, *1*, 1-8.**[crossref], [Google scholar], [Publisher]**
[7] P.Vicini, A. Geronikaki, M. Incerti, B. Busoners, G. Poni, C.A. Cabras, P.L. Colla,*Bioorg. Med. Chem*., **2003,***11*, 4785-4789.**[crossref], [Google scholar], [Publisher]**
[8] S.M. Jadhav, V.A.Shelke, S.G. Shankarwar, A. S. Munde, T.K. Chondhekar,*J.Saudi Chem. Soc.*,**2014,** *18*, 27-34.**[crossref], [Google scholar], [Publisher]**
[9] A.M.Khedr, M. Gaber, R.M. Issa, H.Erten, *Dyes Pigments,***2005** ,*67*, 117-126.**[crossref], [Google scholar], [Publisher]**
[10] R.M. Issa, A.M. Khedr, H. Rizk, *J.Chin. Chem.Soc*., **2008**, *55*, 875-884. **[crossref], [Google scholar], [Publisher]**
[11] A.I Vogel, Text book of practical Organic Chemistry, 5th Ed., Longman, London, **1989**, 400-401.**[Google scholar]**
[12] W. Rehman, Z. Hassan, U. Rashid, F. Rahim, O.U. Rehaman Abid, M. Waseem, *Med. Chem. Res.*, **2014**,*23*, 2207-2211.**[crossref], [Google scholar], [Publisher]**
[13] C. M.da Silva, D. L.da Silva, L. V.Modolo, R.B. Alves, M.A.de Resende, C. V.B.Martins, Â. Fátima, *Adv. Res.*, 2011, *2*, 1, 1-8.**[crossref], [Google scholar], [Publisher]**
[14] D.G. Palke, S.D. Salunke, *Asian J. Chem*., **2017**, *29*, 2167-2170.**[crossref], [Google scholar], [Publisher], [Pdf]**
[15]Spectrometric Identification of Organic compounds, Silverstein, Bassler and Morril 4thEd. John Wiley and Sons, New

York,**1991**.**[crossref], [Google scholar], [Publisher]**
[16] S. Salunke, *Transition Metal Complexes of Dehydro Acetic Acid Schiff Bases*, Lap Lambert Academic Publishing, **2015**, Republic of Moldova, Chisinau-2068, str. A.Russo 15, of.61. **[Publisher]**
[17] D.G. Palke, S.D. Salunke, *Der PharmaChem.*, **2018**, *10*, 46–49.**[Pdf], [Google scholar], [Publisher]**