Synthesis of Schiff's Bases from 2-Amino-4H-1, 3-Oxazine / Thiazine and Substituted Aldehydes and their Transition Metal Complexes

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ABSTRACT

Objective: Many methods can be found in literature for the synthesis a Oxazines and Thiazines. Few are reported for one-pot multi component cyclo-condensation of an alkayane urea / Thiourea and Aldehyde to 2- amino-4H-1, 3-Oxazines or Thiazines. Different catalysts are reported like Trifluoro-acetic acid, glacial acetic acid under reflux condition Mandal and Co-workers have utilized perchloric acid (HClO₄) supported on silica gel as catalyst under solvent free condition ytterbium trifluorate [Yb(OTf)₃] plays role of Lewis acid. It is also used in several Diel's-Alder cyclo-addition reactions.

Inspired these observations, development of simple effective synthetic strategy for the synthesis of 2-amino-4H-1, 3-Oxazium & Thiazines was attempted.

Material and Methods: One pot multi-component synthesis of Schiff's base as new ligand an their complexes with Ni, Fe, Co and Cu and developed using 2-amino-4H-1,3 Oxazines /Thiazines and substituted Aldehydes, different catalyst are used to synthesize of 2-amino 4H-1,3 Oxazines. Its characterization is confirmed by taking IR, NMR spectra.

The Schiff's base act as ligand is bidentate, when it is treated to metal complexes in 1:1 ratio (metal: ligand) complexes are formed.

Result: By using the bioactive molecules like 2-amino-4H-1, 3 Oxazine / Thiazines, Schiff's Bases can be synthesized by using different aldehydes. These Schiff's Bases has antitumor, antipyretic, anti-inflammatory property. And these Schiff's bases treated with bioactive metals like Co, Fe, Cu, Zn which enhances their bio-activity.

Conclusion: All these synthesized Schiff' Bases and their metal complexes having bioactive properties.

KEYWORDS: Coordination complexes and Characterization, Oxazines and substituted aldehydes, Synthesis of Schiff's bases, 2-amine-4H-1, 3.

INTRODUCTION

In chemical research and industry has increased efficient, economical clean short time procedure increases attention in recent years¹. Development of such methods is great demand in coordination chemistry.

Compounds containing an Oxazine or Thaizine moiety have been found to passes a wide range of bioactivities like antifungal antibiotic²⁻³. A derivative of oxazine has also exhibited anti- HIV activity

Many methods can be found in literature for the synthesis a oxazines and thiazines. Few are reported for one-pot multicomponent cyclocondensation of an alkayane urea/thiourea and aldehyde to 2- amino-4H-1, 3-oxazine or thiazine³. Different catalysts are reported like trifluoraoacetic acid glacial acetic acid under reflux condition Mandal and co-workers have utilized perchloric acid (HClO₄) supported on silica gel as catalyst under solvent free condition ytterbium trifluorate [yb(OTf)₃] plays role of Lewis acid It is also used in several Diel's-Alder cyclo-addition reactions⁴.

Inspired these observations, development of simple effective synthetic strategy for the synthesis of 2-amino-4H-1, 3-Oxazine & Thiazine was attempted⁵⁻⁷.

Schiff's bases also have applications of ant-inflammatory, antitumor, antibiotic, antifungal activities. We want to enhance the bioactivity by containing these two moiety using different methods are used⁸⁻⁹. To synthesize the Schiff's bases. Different methods are reported like constant stirring at moderate temperature use of catalysts like H₂SO₄, AlCl₃ etc.

If such bases are treated with biologically active metals like Zn, CO, Cu, Fe it enhance the biological activity of compounds.

Preparation of 2-Amino-4H-1, 3-Oxazine / Thiazine:

A solution of benzaldehyde (1 m mole), (2- bromovinyl) 1 m mole and Urea 3 m mole in water (3 m mole) was taken in 20 ml vial and subject to M.W. irradiated at (120⁰-250⁰C) reaction completed monitored by TLC, reaction mixture was cooled, filter wash with acetone and re-crystallize by ethanol to give pure product.

Table. No.1

Sr. NO.	R ₁	R ₂	X	Yield in %
1	H	C	O	89
2	P-CH ₃	C ₆ H ₅	O	72
3	O-OCH ₃	C ₆ H ₅	O	84
4	M-NO ₂	C ₆ H ₅	O	85
5	H	C ₆ H ₅	S	76
6	P-CH ₃	C ₆ H ₅	S	72
7	P-Cl	C ₆ H ₅	S	77
8	P-NO ₂	C ₆ H ₅	S	66

Preparation of Schiff's bases :

Take m mol of 2- amino 4H-1, 3 Oxazine or Thiazine compound in mortar and add benzaldehyd add 2-3 drops of ethanol grind for 10-15 min or it stir for 1-2 Hrs. We get the products. Pour this product on crushed ice, filter and re-crystallize it using ethanol.

Strong singlet at 9.41 in NMR and 3400-3500 and in IR does no observed indicates NH₂ convert in R₂C = NR (imines) Band at 3650-3584 due to free -OH band at 1689-1471 due to imines stretching

Synthesis of Metal complexes:

Solution of ligand in methanol & metal salt were mixed thoroughly in 1:1 and 2:1 metal legend ratio and 1% mixed KOH solution in methanol was added to adjust PH between 7-8 and reflux for 1-2 hr. We get complex which monitored on TLC.

$M(CH_3COO)_2(H_2O)_4 + 1 \text{ or } 2 \text{ Ln} \rightarrow M \text{ Ln or } M \text{ Ln}_2$

M= Cu, Fe, Co, Zn

Select spectroscopic data Band at 525-425, 450-350 NMR- H Ar. at 7.60

RESULT AND DISCUSSION

By using the bioactive molecules like 2-amino-4H-1, 3 Oxazine / Thiazines, Schiff's Bases can be synthesized by using different substituted aldehydes. These Schiff's Bases has antitumor, antipyretic, anti-inflammatory property.

And these Schiff's bases treated with bioactive metals like Co, Fe, Cu, and Zn which enhances their bio-activity¹⁰⁻¹¹.

Spectral data of 2-Amino-4H-1, 3-oxazine / thiazine:

Sr.No	Name of Compound	Nature	M.P	Result in %	H NMR	IR
1	4,6-Diphenyl-4H-1,3-Oxazine-2-amine	pale yellow crystals	219-221 ⁰ c	89%	9.45 (S,2H,NH ₂), 7.76 (m, J=2Hz,4Hz,2H,Ar), 7.46 (M,3H,HAr), 7.52 (m, J = 2Hz, 4Hz, 8H, HAr) 6.62 (d J = 4Hz, 1H, CH) , 5.58 (d J= 4Hz, 1H, CH)	3400-3500, 3078, 1710, 1664, 1371, 1330, 1263, 1096
2	6-phenyl-4 (P-tolyl) -4H-1-3-oxazine-2-amine	pale yellow crystal	176-178 ⁰ c	84%	9.43 (S,2H,NH ₂), 7.72 (m J =2 Hz, 4Hz ,2H,HAr), 7.46 (m,3H, HAr), 7.28 (d J= 4Hz, 2H, Ar) 7.16 (d,J=4Hz, 2H, HAr), 6.60 (d, J=4Hz, 1H CH) 5.56 (d, J=4Hz, 1H; CH), 2.43 (S, 3H,CH ₃)	3400-3500, 3078, 3100, 1710, 1664, 1371, 1330, 1263, 1096
3	4-(O-Methoxyphenyl)-6-phenyl - 4H-1, 3-Oxazine – 2-amine)	Pale yellow crystal	186-188 ⁰ c	72%	9.42 (Cs 2H, NH ₂), 7.72 (m,J= 2Hz, 4Hz, 2H, HAr) 7.43 (m, J = 2Hz 4Hz, 5H, HAr), 7.22 (d, J = 4Hz) 7.43 (m,J= 2Hz 4Hz, 5H, HAr), 7.22 (d,J=4Hz, 1H, HAr), 7.09 (d J= 4Hz, 1H HAr), 6.61 (d,J= 4Hz.1H CH), 5.54 (d,J=4Hz, 1H CH) 3.87 (S,3H, OCH ₃)	3400-3500, 3078, 3120, 1710, 1650, 1471, 1330, 1247, 1040
4	(m-Nitrophenyl) 6-Pheyl- 4H-13oxazine-2-amine	Pale yellow crystal	168-170 ⁰ c	86%	9.41 (s, 2H NH ₂), 8.21 (m, J= 2Hz, 4Hz, 2H, HAr) 7.99 (m,J =2Hz, 4Hz, 2H, HAr) 7.72 (m.2H, HAr), 6.42 (d,J= 4Hz 1H, CH) 5.55 (d, J= 4Hz, 1H, CH)	3400-3500, 3078, 1710, 1664, 1371, 1330, 1263, 1096
5	4,6-diphenyl-4H-1, 3-Thiazine-2-amine	Pale yellow crystals	178-180 ⁰ c	76%	9.88 (S 2H, NH ₂), 7.42 (M,7H, HAr) 7.38 (M,2H,HAr) , 7.18 (d J=4Hz, 1H, HAr) 6.62 (d,J=2Hz 1H CH) 6.22 (d, J= 2Hz 1 H CH)	3400-3500, 3080, 1523, 1710, 1660, 1371 1330, 1263, 1096

6	6 (phenyl-4(P-Tolyl)-4H-1, 3 thiazin-2-amine	Pale yellow crystal	180-182 ⁰ c	72%	9.86 (S, 2H, NH ₂) 7.41 (d, J= 8Hz, 1H, HAR) 7.34 (d,J= 8Hz, 1H, HAR) , 7.22 (m,7H HAR), 6.71 (d, J= 2Hz, 1H, CH), 6.24 (d,J=2Hz, 1H, CH) 2.42 (S,3H, CH ₃)	3400-3500, 3078, 3100, 1710, 1664, 1371, 1330, 1263, 1096
7	4 (P-Chlorophenyl) -6 phenyl-4 H-1, 3-thiazine-2amine	Pale yellow crystals	170-172 ⁰ c	77%	9.88 (S,2H, NH ₂) 7.42 (m, 4Hz, HAR), 7.32 (m, 2H, HAR) , 6.26 (M, 3H, HAR), 6.72 (d, J = 2Hz 1H CH), 6.40 (d,I= 2Hz, 1H, CH)	3400-3500, 3078, 1720, 1660, 1371, 1330, 1263, 1096

Spectral data of Schiff's bases

Sr. No	Name of Compound	H NMR	IR
1	4,6 – Diphenyl-4H-1, 3 Oxazine-2, imine (2-hydroxyl) benzene	7.76 (m, J = 2Hz, 4Hz, 2H, Ar) , 7.52 (m, J= 2Hz, 4Hz, 8H, HAR) 6.62 (t, J = 4Hz, 1 H CH) 5.58 (d, J= 4Hz, 1H CH), 5.48 (d J = 2Hz 1 H CH), 5.20 (S 1H, OH)	3650-3584, 3080, 1710, 1664, 1470, 1263, 1096
2	6- Phenyl -4 (P-tolyl)- 4H-1-3 Oxazine -2 imine (2-hydroxy) benzene	7.72 (m, J = 2Hz 4Hz, 2H, Ar) 7.46 (m, 3H HAR), 7.28 (d J = 4Hz 2H, HAR) 7.16 (d,J = 4Hz, 2H, HAR), 6.62 (d J = 4Hz, 1H CH) , 5.56 (t ,J=4Hz 1H, CH) 5.48 (d , 2Hz, 1H, CH) 5.20 (S, 1H, OH), 2.43 (S,3H, CH ₃)	3650-3584, 3080, 1710, 1689, 1650, 1470, 1263, 1096
3	4- (O- methoxy phenyl -6 phenyl – 4H,1 3-Oxazine 2- Imine (2-hydroxy) benzene	7.72 (m,J=2Hz, 4Hz, 2H HAR), 7.43 (m,J=2Hz 4Hz, 5H HAR), 7.22 (d, J= 4Hz, 1H, HAR), 7.09 (d J=4Hz, 1H, HAR) 6.61 (d J = 4Hz, 1H CH) 5.54 (d J= 4Hz 1 H CH) 5.48 (d 2H 1H CH) 5.20 (S, 1H, OH), 3.87 (S, 3H, OCH ₃)	3650-3584, 3080, 3120, 1710, 1630, 1471, 1330, 1247, 1040

4	(M-Nitrophenyl) 1- 6 Phenyl-4H-1, 3- Piazome-2 imine (2-hydroxy)benzene	8.21 (m, J = 2Hz, 4Hz, 2H, HAr), 7.99 (m, J = 2z, 4z, 2H, HAr), 7.72 (M, 2H, HAr) , 6.42 (D, J=4z, 1H, CH), 5.55 (d , J – 4Hz, 1H, CH) 5.48 (d, J = 2Hz, 1H CH) , 5.20 (S, 1H, OH)	3650-3584, 3080, 1710, 1630, 1471, 1330, 1247, 1040
5	4, 6 diphenyl-4H-1, 3- thiazine-2 imine (2-Hydroxy) benzene	7.42 (m, 7H, HAr), 7.38 (m, 2H, HAr), 7.18 (d, J = 4Hz, 1H, HAr), 6.62 (d, J = 2Hz, 1H, CH) , 6.22 (d, J=2z, 1H, CH), 5.58 (d, J = 2Hz, 1H, CH) 5.20 (S,, 1H, OH)	3650-3584, 3080, 1710, 1660, 1371, 1330, 1263, 1096
6	6-Phenyl-4 (P-tolyl)-4H-1, 3 -Thiazine-2-imine (2- hydroxy)benzene	7.41 (d, J = 8Hz, 1H, HAr), 7.34 (d, J=8Hz, 1H HAr) 7.22 (m, 7H, HAr) 6.71 (d , J = 2Hz, CH) , 6.24 (d, J= 2Hz, 1H, CH), 5.58 (d J = 2Hz, 1H, CH) 5.20 (S, 1H, OH) 2.42 (S, 3H, CH ₃)	3650-3584, 3078, 3100, 1710, 1664, 1371, 1330, 1263, 1096
7	4 (P.Chlorophenyl) -6 phenyl- 4 H-1, 3-thiazine- 2-imine (2- hydroxy) benzene	7.42 (m, 4H, HAr) 7.32 (m, 2H, HAr), 7.26 (m, 3H, HAr) , 6.72 (d, J= 2Hz 1H CH), 6.60 (d, J = 2Hz 1H CH), 5.50 (d, J= 2Hz, 1H, CH) 5.20 (S, J 1H OH)	3650-3584, 3078, 1710, 1660, 1371, 1330, 1263, 1096
8	4 (P-Nitrophenyl) -6 phenyl- 4 H-1, 3-thiazine- 2-imine (2- hydroxy)benzene	8.32 (m, 2H, HAr) 7.82 (m, 2H, HAr) 7.45 (m, 5H, HAr) 6.67 (d, J= 2Hz, 1H CH) 6.26 (d, J=2Hz, 1H CH), 5.58 (d, J=2Hz 1H CH), 5.20 (S, 1H CH)	3650-3584, 3078, 1710, 1660, 1523, 1371, 1330, 1263, 1096

CONCLUSION

All the synthesized Schiff Bases and their metal complexes having bioactive properties like anti-inflammatory, antitumor, antibiotic, antifungal activities.

REFERENCES

1. Mathew, B.P. Kumar, A.Sharma, S. Shukla, P.K. Nath, M.Eur, J. Med. Chem. 45, 1502 (2010)
2. Haneisi J. : Okazaki, T. Hata , T, Jamura L, Nom. Arura M.J. Antibiot, 24, 797 (1971)
3. Sasaki K. Kusalabe, Y. Esumi, S.J. Antibiot 25, 151 (1972)
4. Pictsh M : Custchow M.J. Med. Chem. 48, 8270 (2005)

5. Hung S. : Pan Y. : Zhu Y : Wu, A. Org, Lett. 7,3797 (2005)
6. Cecchetti, V : Cruciani, G : Filliponi, E : Fravolini A; Tabarrini O, T.Bioorg. Med.Chem. 5, 1339(1997)
7. Remillard, S. Rebhu, L.I Howie, G.A. Kupchan, S.M .Science 189 ,1002 (1975)
8. Sokolova, A,S ; Rayabokon', N.A; Erashova, Yu.A; Andreeva, N.A. ; Nemeryuk, M.P; Kermov, A.F. Traven, N.I; Yadrovskaya, V.A; Chernov, V.A ; Safonova, T.S.Pharm. Chem.J 11 (9) ,49 (1977)
9. Pietsch, M, Gutschow M, M.J.Med.Chem, 48,8270 (2005)
10. Diwagh, S.S; Piste, P.B. Int. J. Pharm. Sci, Res. 4,2045 (2013)
11. Mandal, P.K.Misra, A.K. Lett. Org. Chem. 3, 848 (2006)

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