Available online at www.joac.info

ISSN: 2278-1862

Journal of Applicable Chemistry

2015, 4 (2): 628-632

(International Peer Reviewed Journal)

Short Communication

Synthesis of Novel Schiff's Bases of Substituted Isatins With 5-(Amino methyl)-3-(3-Fluoro-4-Morpholino Phenyl) Oxazolidin-2-One

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Accepted on 27th February 2015

ABSTRACT

Ten derivatives of novel substituted Isatin Schiff's bases ***3(a-j)*** *were synthesized by condensation of substituted Isatins* ***1(a-j)*** *with 5-(aminomethyl)-3-(3-fluoro-4-morpholinophenyl) oxazolidin-2-one (Linazolide)* ***2*** *in methanol and added a catalytic amount of acetic acid. All structures of the newly synthesized compounds were confirmed by IR, NMR, mass spectral studies and elemental analyses.*

Keywords: Isatin, Schiff's bases, condensation, methanol.

INTRODUCTION

Isatins and their derivatives are well known to posses varied biological activities such as antibacterial [1–3], antifungal [1, 3–5], anticonvulsant [2, 6], anti-HIV [7], anticancer [1, 2], antiviral [1], and enzyme inhibitors [2]. In addition, the oxazolidinones are an important class of molecular architectures found in a broad range of synthetically and biologically interesting compounds. They have novel mechanism of action that involves the inhibition of bacterial protein synthesis at a very early stage prior to chain inhibition [8]. Linezolid is a successful agent of this class and has already gained the permission of the FDA and come into the market. Referring to the structure activity relationship studies, we have reported a very simple method for the synthesis of novel Schiff's bases from substituted Isatins with linezolid.

MATERIALS AND METHODS

All the melting point is uncorrected. The purity was checked by thin layer chromatography with silica gel 60 GF254 Merck pre-coated plates (0.25 mm) was visualized using UV. 0.1 for flash chromatography on silica gel (particle size 100-200 mesh) and characterized by spectral studies. The IR spectra were recorded on Shimadzu FTIR model 8010 spectrophotometer and are given in cm^{-1} in KBr. The ^{1}HNMR & ^{13}CNMRspectra were recorded on Bruker AM-400 NMR spectrometers in $CDCl_3$ and DMSO-d_6. The

chemical shifts are reported in δ (ppm) relative to tetramethylsilane as internal standard. Mass spectra analyses performed with an Agilent 6400 Series equipped with an electrospray ionization source.

General method for the synthesis of Schiff's bases 3(a-j): Dissolved the compounds of substituted Isatins **1(a-j)** (0.01 mol) and 5-(aminomethyl)-3-(3-fluoro-4-morpholinophenyl) oxazolidin-2-one **2** (0.01mol) in 60 mL of methanol than added a catalytic amount of glacial acetic acid. The reaction mixture heated to reflux for about 30-42 h (monitored by TLC). After completion of the reaction, the reaction mixture poured into ice- cold water, solid separated, filtered and dried. The compounds were purified by re-crystallization with methanol.

3-[3-(3-Fluoro-4-morpholin-4-yl-phenyl)-2-oxo-oxazolidin-5-yl-methyl imino]-1,3-dihydro-indol-2-one (3a): Yield:75%; M.P:145-148 ^oC; IR(cm^{-1}): 3397, 3027, 2953, 2827, 1738, 1675, 1627,1237, 1049; ^1H NMR(DMSO-d_6): 2.76 (m,4H); 3.06-3.43 (m,2H); 3.65-3.98 (m,6H); 4.53 (m,1H); 6.52 (dd,1H); 7.00-7.05 (dd,1H); 7.20 (s,1H);7.25-7.30 m,2H);7.60-7.69 (m,2H); 9.02(s,1H); ^{13}C NMR: 168.0, 163.1, 156.5, 153, 146.9, 133,130.2,131.3,130,124.8, 124, 122, 120, 116.3, 111.0, 83.6, 66.5, 50.2,46,4,45.9; Mass (m/z): 425.16 (M+1); Anal. Calcd. for $C_{22}H_{21}FN_4O_4$: C: 62.26; H: 4.99; N:13.20; Found: C: 62.18; H: 4.87; N:13.02.

5-Chloro-3-[3-(3-Fluoro-4-morpholin-4-yl-phenyl)-2-oxo-oxazolidin-5-yl-methylimino]-1,3-dihydro-indol-2-one(3b): Yield:52%;M.P:172-174^oC;IR(cm^{-1}):3355, 3025, 2950, 2829, 1740, 1680, 1627,1234,1050,880; ^{1}HNMR (DMSO-d_6) :2.83 (m,4H); 3.04-3.42 (m,2H); 3.66-3.95 (m,6H); 4.63 (m,1H); 6.58 (dd,1H); 7.17 (s,1H); 7.23-7.28 (m,2H); 7.63 (s, 2H); 8.56(s,1H); ^{13}CNMR (DMSO-d_6): 167.8, 162.6, 156, 153.5, 144.8, 133.0, 132.1, 131.3, 130.2, 125.8, 123.2, 121.6, 120.3, 118.3, 112.0, 83.6, 66.3, 49.8, 46,4, 46.0; Mass (m/z): 459.16(M+1); Anal. Calcd. for $C_{22}H_{20}ClFN_4O_4$: C: 57.58; H: 4.39; N:12.21; Found: C: 57.82; H: 3.98; N:12.30.

5-Bromo-3-[3-(3-Fluoro-4-morpholin-4-yl-phenyl)-2-oxo-oxazolidin-5-yl-methylimino]-1,3-dihydro-indol-2-one (3c): Yield: 68%; M.P: 165-167 ^oC; IR (cm^{-1}): 3405, 3030, 2955, 2830, 1735, 1665 1627, 1235, 1025. 990; ^{1}HNMR (DMSO-d_6):2.63 (m, 4H); 3.00-3.32 (m, 2H); 3.61-3.85(m, 6H); 4.58 (m, 1H); 6.55 (dd, 1H); 7.20 (s, 1H); 7.45-7.58(m, 2H); 7.77(s, 2H); 8.63(s, 1H);^{13}CNMR(DMSO-d_6):167.5, 162.3, 156.2, 153.4, 145.9, 133.3, 134.1, 130.2, 126.5, 123.6, 120.0, 118.2, 116.4, 111.3, 83.3, 66.5, 49.3, 46,8, 46.3; Mass (m/z): 504.36(M+1), 506.32(M+2); Anal. Calcd. for $C_{22}H_{20}$ $BrFN_4O_4$: C: 52.50; H: 4.01; N:11.13; Found: C: 53.12; H: 3.96; N:11.80.

5-Nitro-3-[3-(3-Fluoro-4-morpholin-4-yl-phenyl)-2-oxo-oxazolidin-5-yl-methyl imino]-1,3-dihydro-indol-2-one(3d): Yield: 42%; M.P:155-158 ^oC; IR (cm^{-1}): 3390, 3023, 2951, 2834, 1740, 1675, 1630, 1543, 1430, 1328, 1230, 1052;^{1}HNMR (DMSO-d_6):3.02 (m,4H); 3.63-3.95 (m,6H); 4.62(m,1H);6.55 (dd,1H);7.20-7.28(m,2H); 7.90-7.95 (m,1H); 8.23 (m, 1H); 8.55 (s,1H), 9.23 (s,1H); ^{13}C NMR (DMSO-d_6):168.5,163.3, 156.5, 153.4, 152.8, 144.3, 132.8, 130.2, 124.9, 124.2, 123.4, 123.2, 118.2, 116.4, 111.2, 83.5, 66.2, 46.5, 46.3; Mass (m/z): 470.14(M+1); Anal. Calcd. for $C_{22}H_{20}FN_5O_6$: C: 56.29; H: 4.29; N:14.92; Found: C: 56.12; H: 4.16; N:14.93.

5-Fluoro-3-[3-(3-Fluoro-4-morpholin-4-yl-phenyl)-2-oxo-oxazolidin-5-yl-methylimino]-1,3-dihydro-indol-2-one (3e): Yield: 58%; M.P: 168-170^oC; IR (cm^{-1}):3400, 2960, 2829, 1741, 1670,1631, 1450, 1238,1049.1000; ^{1}HNMR(DMSO-d_6):2.83(m,4H); 3.05-3.42 (m,2H); 3.68-3.95(m,6H); 4.58 (m,1H); 6.55 (dd,1H); 6.98 (m,1H); 7.23-7.26 (m,2H); 7.35(s,1H); 7.63-7.65 (m,1H), 9.13(s,1H); ^{13}CNMR:(DMSO-d_6): 167.8, 162.8, 158.8,155.6,153.3,142.9,132.8, 130.2, 125.5,123.3,118.2, 118.0, 116.1, 114.3, 111.2, 83.8, 66.7, 49.2, 46,5, 46.1. Mass (m/z): 443.15(M+1); Anal. Calcd. for: $C_{22}H_{20}F_2N_4O_{4::}$ C: 59.73; H: 4.56; N:12.66; Found: C: 59.68; H: 3.98; N:12.30.

5-Methyl-3-[3-(3-Fluoro-4-morpholin-4-yl-phenyl)-2-oxo-oxazolidin-5-yl-methylimino]-1,3-dihydro-indol-2-one (3f): Yield:63%; MP:155-157^{o}C;IR (cm^{-1}): 3402, 2951, 2828, 1740, 1680, 1629, 1452, 1238, 1044; ^{1}HNMR (DMSO-d_6): 2.40 (s,3H), 2.95 (m,4H); 3.12-3.46 (m,2H); 3.65-3.93 (m,6H);4.60 (m,1H);6.58 (dd,1H);7.10 (m,1H);7.20-7.25 (m,2H); 7.43(s,1H); 7.65 (s,1H), 8.88 (s,1H); ^{13}CNMR (DMSO-d_6): 167.7, 162.4, 156.2, 153.2, 144.0, 139.5, 133.2, 132.1,130.6, 129.8, 124.2, 121.8, 118.4,116.5, 111.0, 83.4, 66.8, 46.2, 45.8, 24.6; Mass (m/z): 439.18(M+1); Anal. Calcd. for $C_{23}H_{23}FN_4O_4$: C: 63.00; H: 5.29; N:12.78; Found: C: 62.88; H: 5.12; N:12.69.

6-Chloro-3-[3-(3-Fluoro-4-morpholin-4-yl-phenyl)-2-oxo-oxazolidin-5-yl-methylimino]-1,3-dihydro-indol-2-one(3g): Yield: 53%, M.P:160-162^{o}C; IR (cm^{-1}): 3355, 3025, 2950, 2829, 1730, 1670, 1630, 1200, 1050, 865; ^{1}HNMR (DMSO-d_6): 2.93 (m,4H);3.12-3.46 (m,2H);3.63-3.91 (m,6H); 4.55 (m,1H); 6.56 (dd,1H); 7.04 (m,1H); 7.20-7.27 (m,2H); 7.54 (m, 1H); 7.68 (s,1H); 9.02 (s,1H);^{13}C NMR (DMSO-d_6):167.3,163.0,155.8,153.3, 145.8, 133, 132.3, 131.6, 130.4, 126.0, 123.1, 121.6, 120.8, 118.1, 111.5, 83.4, 66.4, 50, 46,3, 46.1; Mass (m/z): 460.11(M+1),462.12(M+2); Anal. Calcd. for $C_{22}H_{20}ClFN_4O_4$: C: 57.58; H: 4.38; N:12.21; Found: C: 58.02; H: 3.66; N:12.68. Anal. Calcd. for: C: 57.58; H: 4.39; N:12.21; Found: C: 57.82; H: 3.98; N:12.30.

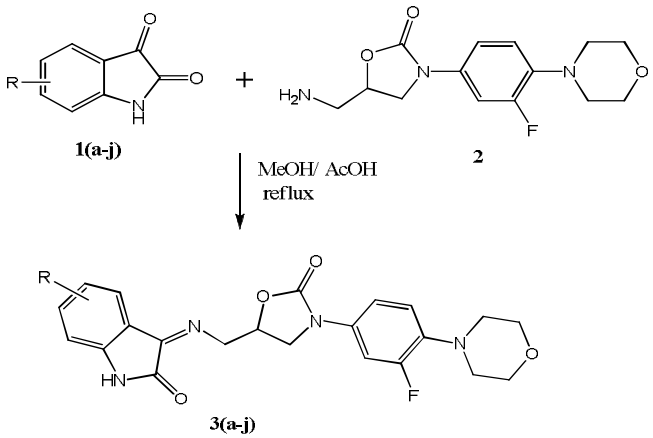
6-Bromo-3-[3-(3-Fluoro-4-morpholin-4-yl-phenyl)-2-oxo-oxazolidin-5-yl-methylimino]-1,3-dihydro-indol-2-one (3h): Yield:72%, M.P:158-160^{o}C;IR (cm^{-1}): 3385, 3026, 2955, 2840,1742, 1673, 1628, 1220, 1025, 992; ^{1}H NMR(DMSO-d_6):2.83 (m,4H); 3.08-3.33 (m,2H); 3.66-3.90 (m,6H); 4.62 (m,1H); 6.55 (dd,1H); 7.20-7.25 (m,3H); 7.45-7.50 (m,1H); 7.80 (s, 1H); 9.12 (s,1H);^{13}C NMR(DMSO-d_6):168.5, 162.5, 155.2, 153.2, 146.2, 133.0, 134.3, 129.6, 126.3, 124.2, 119.8, 118.0, 116.2, 111.0, 83.3, 66.4, 50.2, 46,4, 46.2; Mass (m/z): 504.3(M+1), 506.3(M+2); Anal. Calcd. for $C_{22}H_{20}BrFN_4O_4$: C: 52.50; H: 4.01; N:11.13; Found: C: 52.41; H: 3.96; N:11.75.

6-Fluoro-3-[3-(3-Fluoro-4-morpholin-4-yl-phenyl)-2-oxo-oxazolidin-5-yl-methylimino]-1,3-dihydro-indol-2-one(3i): Yield:53%; M.P:172-174^{o}C;IR(cm^{-1}): 3395, 3000, 2840, 1742, 1665, 1617, 1500, 1238, 1049, 1002;^{1}HNMR(DMSO-d_6):2.90 (m,4H); 3.00-3.32 (m,2H); 3.7-4.00 (m,6H); 4.60 (m,1H); 6.55 (dd,1H); 6.78 (m,1H); 7.18-7.26 (m,2H); 7.38(s,1H); 7.53-7.58 (m,1H), 9.00 (s,1H) ^{13}CNMR(DMSO-d_6):166.8, 163.8, 157.8, 156.6, 153.3, 143.0, 133.0, 131.8, 125.7, 123.8, 118.8, 118.1, 116.6, 114.0, 111.0, 83.3, 66.4, 49.5, 46,4, 46.2; Mass (m/z): 443.15(M+1); Anal. Calcd. for: $C_{22}H_{20}F_2N_4O_4$: C: 59.73; H: 4.56; N:12.66; Found: C: 60.00; H: 4.32; N:12.58.

5,6-Dibromo-3-[3-(3-Fluoro-4-morpholin-4-yl-phenyl)-2-oxo-oxazolidin-5-yl-methylimino]-1,3-dihydro-indol-2-one(3j): Yield:55%, M.P:162-165^{o}C;IR(cm^{-1}): 3390, 3015, 2943, 2840, 1740, 1680, 1620, 1237, 1000,996;^{1}HNMR(DMSO-d_6):2.93(m,4H);3.10-3.43(m,2H);3.70-3.93(m,6H).4.55(m,1H), 6.57 (dd,1H);7.17-7.27(m, 2H); 7.60(s,1H); 7.76(s, 1H); 9.05(s,1H);^{13}CNMR(DMSO-d_6): 167.8, 162.1, 156.0, 153.2, 148.4, 135.1, 132.9, 130.2, 128.6, 125.3,123.3, 121.7, 118.1, 115.9, 111.0, 83.3, 66.3, 49.5, 46,6, 46.0; Mass (m/z): 582.9(M+1),580.9(M-2), 584.9(M+2) ; Anal. Calcd. for $C_{22}H_{19}Br_2FN_4O_4$: C: 45.38; H: 3.29; N:9.62; Found: C: 45.30; H: 3.21; N:9.54.

RESULTS AND DISCUSSION

The synthetic strategies adopted for the synthesis of the target compounds are depicted in **Scheme-1**.After investigating published methods we synthesized title compounds from substituted Isatins. The Isatins **1(a-j)** were condensed with 5-(aminomethyl)-3-(3-fluoro-4-morpholinophenyl)oxazolidin-2-one(Linazolide) **2** in methanol and added a catalytic amount of acetic acid to give corresponding desired compounds **3(a-j)**. The structures of all the newly synthesized compounds were elucidated on the basis of their spectral (IR, NMR and mass) and elemental analyses data.



R=H, Cl, Br, F, $-CH_3$, $-NO_2$ (3a-j)

Scheme-1

APPLICATIONS

The Novel Schiff bases synthesized in my research work are used for preparation of various metal complexes which were used further to study oxygen carrier properties and also to study antimicrobial and anticancer activity.

CONCLUSIONS

We herein in reported the synthesis of novel Schiff's base derivatives of different substituted isatins with 5-(aminomethyl)-3-(3-fluoro-4-morpholinophenyl) oxazolidin-2-one. The synthesized compounds were characterized by ^{1}H NMR, ^{13}C NMR, CHN analysis, FTIR and Mass spectroscopic techniques. All these found to be in accordance with the required data.

ACKNOWLEDGEMENT

I am thankful to Optimus Pharma Ltd., Hyderabad, providing me an opportunity to do my research work. I express my deep sense of gratitude to my research guide Prof. Mukanti and Dr. B. Prasanna for timely guiding me to complete the target molecules, and also grateful to my research colleagues.

REFERENCES

[1] G. Cerhiaro, A. M. D. Ferreira, Oxindoles and copper complexes with oxindole-derivatives as potential pharmacological agents, *Journal of the Brazilian Chemical Society*, **2006**, 17(8), 1473-1485.
[2] S. N. Pandeya, S. Smitha, M. Jyoti, S. K. Sridhar, Biological activities of isatin and its derivatives, *Acta. Pharmaceutica*, **2005**, 55, 27-46.
[3] V. K. Sharma, S. Srivastava, A. Srivastava, Novel coordination complexes of the trivalent ruthenium, rhodium and iridium with hydrazones derived from isatin hydrazide and various aldehydes with spectral and biological characterization, *Polish Journal of Chemistry,* **2006**, 80, 387–396.
[4] V. K. Sharma, A. Srivastava, S. Srivastava, Synthetic, structural and antifungal studies of coordination compounds of Ru(III), Rh(III) and Ir(III) with tetradentate Schiff bases, *Journal of the Serbian Chemical Society*, **2006**, 71(8-9), 917–928.

[5] R. M. Abdel Rahman, Z. El Gendy, M. B. Mahmoud, Synthesis of some new 3-substituted 1,2,4-triazino-indole derivatives and related compounds of potential antifungal activity, *Indian Journal of Chemistry B*, **1990**, 29, 352–358.
[6] S. N. Pandeya, A. S. Raja, J. P. Stables, Synthesis of isatin semicarbazones as novel anticonvulsants-role of hydrogen bonding, *Journal of Pharmacy and Pharmaceutical Sciences*, **2002**, 5(3), 266–271.
[7] T. R. Bal, B. Anand, P. Yogeeswari and D. Sriram, "Synthesis and evaluation of anti-HIV activity of isatin β-thiosemicarbazone derivatives," *Bioorganic and Medicinal Chemistry Letters*, **2005,** 15(20), 4451–4455.
[8] D.C. Eustic, P. A. Feldman, I. Zajac, A.M. Slee, Mechanism of action of Du P 721; Inhabitation of an early event during initiation of protein synthesis, Antimicrob Agents, *chemother*, **1998**, 32, 1218-1222.