ISSN No:-2456-2165

A Synthesis and Biological Evaluation of Indole Derivatives

Mamta H. Chauhan[1,*], Nilesh L. Solanki[2], Dhananjay K. Pandya[3]
Government Science College Veraval, Gir Somnath-362265, India

Abstract:- Oxoindolines are interesting heterocyclic compounds which show diverse biological significance. In this oxoindolines was prepared by one-pot condensation reaction of isatin, dimedone, and various active methylene using piperidine as a basic catalyst and solvent as methanol, under stirring at ambient temperature. The final products were characterized by FT-IR spectroscopy, Mass-spectroscopy, ^{1}H NMR-spectroscopy and ^{13}C NMR-spectroscopy.

Keywords:- *MCRS, Isatin, Dimedone, Oxoindolines, Antimicrobial Estimation.*

I. INTRODUCTION

Bayer created the first spiran, in 1900 defined as a bicyclic hydrocarbon coupled by a single carbon. The term spirocyclanes was used to describe the family of such hydrocarbon.

The chemistry of spiroindoles in which an indole ring is joined to S and N at the C-3 position through a spiro carbon atom is of big interest due to their physiological activities.[1,2,3] spiroindoles having cyclic nature fused at a central carbon are of recent interest due to their interesting conformational features and their structural effects on biological systems. The asymmetric characteristic of molecules due to the chiral-C is one of the significant criteria of biological activities.[4,5]

Spiro-indoles which is present and single unit preparative difficult challenges; whether every ring contributing to its actual structure is either single or identical to the spiro-ring fusion combination which provides a highly useful method of increasing molecular complexity as well as it may offer very big benefit than the introduction of flat and small aromatic rings. New evolution of novel and unrepoted synthetic preparative routes to build the spiro building blocks will definitely facilitate the combination of spiro intermediates into more pharmaceutically active moieties. THE Spiro ring containing organic systems were not only have big three dimensionality i.e. stereospecific than flat aromatic rigs but it introduce the structural uniqueness which is novel.

The spiro-oxindoles is the core intermediate structure of so many pharmacological as well as naturally occurring calkaloids.[6,7] Spiro-oxindoles, specially those which are spiro annulated with hetero-cyclic compounds at the third position have shown highly significant pharmaceutical and biological activities. [8] These physical and chemical properties have been encouraged too many efforts toward the preparation of spiro-oxindole and fused hetero-cycles for the preparation of the diversely structured spiro-cyclic-oxindoles. [9,10] The organic and heterocyclic compound named Isatin is one of the most widely applicable reagent for raising the spiro-oxindoles in number of organic and inorganic reactions such as cyclo-addition, Morita-Baylis-Hillman reaction and other condensation reactions. [11-13] In the before few years, the multi-component reactions which are based on the versatile reactivity of isatins for the preparation of ery numerous spiro-oxindoles. [14,15]

- *General procedure for the synthesis of indole derivatives (CM 01-10)*

A mixture of the isatin or substituted isatin (0.01 mol), substituted active methylene (0.01 mol) and dimedone (0.01 mol) was stirred 2-3 hr. in 20 ml of MeOH with catalytic amount of piperidine. After completion of reaction, reaction mixture was filtered to form the solid white crystalline products (CM 01-10), which was recrystallized from EtOH. The characterizations of synthesized compounds was carried out using Mass, IR, ^{1}H NMR, ^{13}C NMR and elemental analyses. Physical parameters such as melting points, % yield and R_f values of the final compounds are depicted in Table No.1.

- *Spirooxindoles (CM-01)*

Yield: 82%; mp 273-275 ºC; IR (cm^{-1}): 3140 (=C-H str. of aromatic ring), 2962, 2877 (C-H str. of alkane), 2191 (CN str. of cyanide), 1720 (C=O str. of carbonyl of ketone), 1658 (C=O str. of carbonyl of amide), 1604 (C=C str. of aromatic ring), 1465, (C-H bending of alkane), 1219 (C-C str. of alkane), 748 (C-C bending of *o*-di-substituted aromatic ring), 678 (C-H bending of *o*-di-substituted aromatic ring); ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm: 0.99 (s, 6H, H_a), 2.07-2.19 (s, 2H, H_b), 2.49-2.60 (m, 2H, H_c), 6.77-6.79 (d, 1H, H_d), 6.86-6.90 (t, 1H, H_e), 6.96-6.98 (d, 1H, H_f), 7.11-7.15 (m, 2H, H_g), 7.22 (s, 2H, H_h), 10.39 (s, 1H, H_i); ^{13}C NMR (DMSO-d_6, 400 MHz) δ ppm: 26.99, 27.57, 31.73, 31.91, 38.86, 39.07, 39.28, 39.48, 39.69, 36.90, 40.11, 46.78, 48.58, 49.96, 57.46, 109.20, 110.76, 117.30, 121.64, 122.98, 128.13, 134.38, 142.03, 158.73, 164.10, 177.99, 194.84; MS: *m/z* 335; Anal. Calcd for $C_{19}H_{17}N_3O_3$: C, 68.05; H, 5.11; N, 12.53%; Found: C, 68.17; H, 5.20; N, 12.61%.

- *Spirooxindoles (CM-02)*

Yield: 78%; mp 268-270 ºC; IR (cm^{-1}): 3109, 3178 (=C-H str. of aromatic ring), 2955, 2870 (C-H str. of alkane), 2337 (CN str. of cyanide), 1720 (C=O str. of carbonyl of ketone), 1689 (C=O str. of carbonyl of amide), 1612,1527 (C=C str. of aromatic ring), 1473, (C-H bending of alkane), 1226 (C-C str. of alkane), 1296, 1311 (C-O str. of ester), 1049, 1026 (C-O-C str. of ester), 748 (C-C bending of *o*-di-substituted aromatic ring), 678 (C-H bending of *o*-di-substituted aromatic ring); ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm: 0.77-0.81 (t, 3H, H_a), 0.94 & 1.01 (s, 6H, H_b),

1.99-2.17 (m, 2H, $H_{c,d}$), 2.46-2.60 (m, 1H, H_e), 3.68-3.71 (q, 2H, H_f), 6.66-6.68 (d, 1H, H_g), 6.73-6.77 (t, 1H, H_h), 6.82-6.84 (d, 1H, H_i), 7.02-7.05 (t, 1H, H_j), 7.87 (s, 1H, H_k), 10.15 (s, 1H, H_l); ^{13}C NMR (DMSO-d_6, 400 MHz) δ ppm:13.07, 26.64, 27.76, 31.52, 38.83, 39.04, 39.25, 39.49, 39.67, 39.88, 40.09, 46.57, 50.60, 58.81, 76.27, 108.09, 113.05, 120.51, 122.20, 127.14, 135.95, 144.00, 159.08, 162.38, 167.62, 179.78, 194.63; MS: *m/z* 382; Anal. Calcd for $C_{21}H_{22}N_2O_5$: C, 65.96; H, 5.80; N, 7.33%; Found: C, 66.07; H, 5.93; N, 7.42%.

➢ *Spirooxindoles (CM-03)*

Yield: 89%; mp 281-283 ºC; IR (cm^{-1}): 3155 (=C-H str. Of aromatic ring), 2955, 2870 (C-H str. Of alkane), 2191 (CN str. Of cyanide), 1728 (C=O str. Of carbonyl of ketone), 1658 (C=O str. Of carbonyl of amide), 1604 (C=C str. Of aromatic ring), 1473, (C-H bending of alkane), 1350 (C-N str. Of amine), 1219 (C-C str. Of alkane), 810 (C-H bending of p-di-substituted aromatic ring), 686, 632 (C-H bending of o-di-substituted aromatic ring), 547 (C-Br str. Of halogen); ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm: 1.02 (s, 6H, H_a), 2.15 (s, 2H, H_b), 2.57 (s, 2H, H_c), 6.76 (s, 1H, H_d), 7.21 (d, 2H, H_e, H_f), 7.33 (s, 2H, H_g), 10.56 (s, 1H, H_h); ^{13}C NMR (DMSO-d_6, 400 MHz) δ ppm: 27.15, 27.50, 31.96, 38.85, 39.06, 39.27, 39.48, 39.69, 39.89, 40.10, 47.01, 49.90, 56.68, 110.15, 111.16, 113.29, 117.20, 125.93, 130.90, 136.77, 141.42, 158.84, 164.60, 177.65, 195.09; MS: m/z 413; Anal. Calcd for $C_{19}H_{16}BrN_3O_3$: C, 55.09; H, 3.89; N, 10.14%; Found: C, 55.18; H, 3.99; N, 10.25%.

➢ *Spirooxindoles (CM-04)*

Yield: 76%; mp 271-273 ºC; IR (cm^{-1}): 3155 (=C-H str. of aromatic ring), 2955, 2877 (C-H str. of alkane), 2119 (CN str. of cyanide), 1728 (C=O str. of carbonyl of ketone), 1681 (C=O str. of carbonyl of amide), 1604 (C=C str. of aromatic ring), 1473, (C-H bending of alkane), 1219 (C-C str. of alkane), 1296 (C-O str. of ester), 1057, 1026(C-O-C str. of ester), 810 (C-H bending of *p*-di-substituted aromatic ring), 686, 624 (C-H bending of *o*-di-substituted aromatic ring), 563 (C-Br str. of halogen); ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm: 0.827 (s, 6H, H_a), 0.97&1.00 (s, 4H, H_b), 2.11-2.51 (m, 3H, H_c), 3.36-3.73 (m, 2H, H_d), 6.65 (s, 1H, H_e), 7.01(d, 1H, H_f), 7.22(d, 1H, H_g), 7.95 (s, 2H, H_h), 10.33 (s, 1H, H_i); ^{13}C NMR (DMSO-d_6, 400 MHz) δ ppm: 13.10, 27.07, 27.39, 31.55, 38.85, 39.06, 39.26, 39.47, 39.68, 39.89, 40.08, 46.82, 50.52, 58.96, 75.62, 109.98, 112.03, 112.45, 125.03, 129.83, 138.49, 143.52, 159.17, 162.90, 167.41, 179.38, 194.86; MS: *m/z* 460; Anal. Calcd for $C_{21}H_{21}BrN_2O_5$: C, 54.68; H, 4.59; N, 6.07%; Found: C, 54.79; H, 4.70; N, 6.19%.

➢ *Spirooxindoles (CM-05)*

Yield: 84%; mp 275-277 ºC; IR (cm^{-1}): 3155 (=C-H str. Of aromatic ring), 2955, 2877 (C-H str. Of alkane), 2119 (CN str. Of cyanide), 1728 (C=O str. Of carbonyl of ketone), 1681 (C=O str. Of carbonyl of amide), 1604 (C=C str. Of aromatic ring), 1473, (C-H bending of alkane), 1219 (C-C str. Of alkane), 1296 (C-O str. Of ester), 1057, 1026(C-O-C str. Of ester), 810 (C-H bending of *p*-di-substituted aromatic ring), 683 (C-H bending of *o*-di-substituted aromatic ring), 645 (C-Cl str. Of halogen); ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm: 0.99 (s, 6H, H_a), 2.37 (s, 2H, H_b), 2.49-2.60 (m, 2H, H_c), 7.22-7.24 (d, 1H, H_d), 7.47 (s, 1H, H_e), 7.66-7.68 (d, 1H, H_f), 7.21 (s, 2H, H_g), 10.40 (s, 1H, H_h); ^{13}C NMR (DMSO-d_6, 400 MHz) δ ppm: 21.3, 26.6, 30.4, 44.3, 54.1, 68.2, 111.3, 112.7, 127.9, 129.6, 130.4, 137.6, 140.5, 182.1, 208.3; MS: *m/z* 369; Anal. Calcd for $C_{19}H_{16}ClN_3O_3$: C, 61.71; H, 4.36; N, 11.36%; Found: C, 61.63; H, 4.24; N, 11.46%.

➢ *Spirooxindoles (CM-06)*

Yield: 75%; mp 272-274 ºC; IR (cm^{-1}): 3155 (=C-H str. of aromatic ring), 2955, 2877 (C-H str. of alkane), 2119 (CN str. of cyanide), 1728 (C=O str. of carbonyl of ketone), 1681 (C=O str. of carbonyl of amide), 1604 (C=C str. of aromatic ring), 1473, (C-H bending of alkane), 1219 (C-C str. of alkane), 1296 (C-O str. of ester), 1057, 1026(C-O-C str. of ester), 810 (C-H bending of *p*-di-substituted aromatic ring), 686, 624 (C-H bending of *o*-di-substituted aromatic ring), 645 (C-Cl str. of halogen); ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm: 0.827 (s, 6H, H_a), 0.97&1.00 (s, 4H, H_b), 2.11-2.51 (m, 3H, H_c), 3.36-3.73 (m, 2H, H_d), 6.65 (s, 1H, H_e), 7.01(d, 1H, H_f), 7.22(d, 1H, H_g), 7.95 (s, 2H, H_h), 10.33 (s, 1H, H_i); ^{13}C NMR (DMSO-d_6, 400 MHz) δ ppm: 14.1, 26.6, 30.4, 40.8, 44.2, 54.1, 60.8, 68.7, 111.3, 114.1, 127.9, 129.6, 130.4, 137.6, 140.5, 164.5, 182.1, 208.3; MS: *m/z* 416; Anal. Calcd for $C_{21}H_{21}ClN_2O_5$: C, 60.51; H, 5.08; N, 6.72%; Found: C, 60.43; H, 5.19; N, 6.83%.

➢ *Spirooxindoles (CM-07)*

Yield: 68%; mp 278-280 ºC; IR (cm^{-1}): 3155 (=C-H str. of aromatic ring), 2955, 2870 (C-H str. of alkane), 2191 (CN str. of cyanide), 1728 (C=O str. of carbonyl of ketone), 1658 (C=O str. of carbonyl of amide), 1604 (C=C str. of aromatic ring), 1473, (C-H bending of alkane), 1350 (C-N str. of amine), 1219 (C-C str. of alkane), 810 (C-H bending of p-di-substituted aromatic ring), 686, 632 (C-H bending of o-di-substituted aromatic ring), 547 (C-Br str. of halogen); ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm: 1.02 (s, 6H, H_a), 2.15 (s, 2H, H_b), 2.57 (s, 2H, H_c), 6.76 (s, 1H, H_d), 7.21 (d, 2H, H_e, H_f), 7.33 (s, 2H, H_g), 10.56 (s, 1H, H_h); ^{13}C NMR (DMSO-d_6, 400 MHz) δ ppm: 27.15, 27.50, 31.96, 38.85, 39.06, 39.27, 39.48, 39.69, 39.89, 40.10, 47.01, 49.90, 56.68, 110.15, 111.16, 113.29, 117.20, 125.93, 130.90, 136.77, 141.42, 158.84, 164.60, 177.65, 195.09; MS: m/z 413; Anal. Calcd for $C_{19}H_{16}BrN_3O_3$: C, 55.09; H, 3.89; N, 10.14%; Found: C, 55.18; H, 3.99; N, 10.25%.

➢ *Spirooxindoles (CM-08)*

Yield: 67%; mp 269-271 ºC; IR (cm^{-1}): 3155 (=C-H str. of aromatic ring), 2955, 2877 (C-H str. of alkane), 2119 (CN str. of cyanide), 1728 (C=O str. of carbonyl of ketone), 1681 (C=O str. of carbonyl of amide), 1604 (C=C str. of aromatic ring), 1473, (C-H bending of alkane), 1219 (C-C str. of alkane), 1296 (C-O str. of ester), 1057, 1026(C-O-C str. of ester), 810 (C-H bending of *p*-di-substituted aromatic ring), 686, 624 (C-H bending of *o*-di-substituted aromatic ring), 563 (C-Br str. of halogen); ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm: 0.827 (s, 6H, H_a), 0.97&1.00 (s, 4H, H_b), 2.11-2.51 (m, 3H, H_c), 3.36-3.73 (m, 2H, H_d), 6.65 (s, 1H, H_e), 7.01(d, 1H, H_f), 7.22(d, 1H, H_g), 7.95 (s, 2H, H_h), 10.33 (s, 1H, H_i); ^{13}C NMR (DMSO-d_6, 400 MHz) δ ppm: 13.10, 27.07, 27.39, 31.55, 38.85, 39.06, 39.26, 39.47, 39.68, 39.89, 40.08, 46.82, 50.52, 58.96, 75.62, 109.98, 112.03, 112.45, 125.03, 129.83, 138.49, 143.52, 159.17, 162.90, 167.41, 179.38, 194.86; MS: *m/z* 460; Anal. Calcd for $C_{21}H_{21}BrN_2O_5$: C, 54.68; H, 4.59; N, 6.07%; Found: C, 54.79; H, 4.70; N, 6.19%.

➢ *Spirooxindoles (CM-09)*

Yield: 68%; mp 286-288 ºC; IR (cm^{-1}): 3155 (=C-H str. of aromatic ring), 2955, 2877 (C-H str. of alkane), 2119 (CN str. of cyanide), 1728 (C=O str. of carbonyl of ketone), 1681 (C=O str. of carbonyl of amide), 1604 (C=C str. of aromatic ring), 1473, (C-H bending of alkane), 1219 (C-C str. of alkane), 1296 (C-O str. of ester), 1057, 1026(C-O-C str. of ester), 810 (C-H bending of *p*-di-substituted aromatic ring), 683 (C-H bending of *o*-di-substituted aromatic ring), 645 (C-Cl str. of halogen); ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm: 0.99 (s, 6H, H_a), 2.37 (s, 2H, H_b), 2.49-2.60 (m, 2H, H_c), 7.22-7.24 (d, 1H, H_d), 7.47 (s, 1H, H_e), 7.66-7.68 (d, 1H, H_f), 7.21 (s, 2H, H_g), 10.40 (s, 1H, H_h); ^{13}C NMR (DMSO-d_6, 400 MHz) δ ppm: 21.3, 26.6, 30.4, 44.3, 54.1, 68.2, 111.3, 112.7, 127.9, 129.6, 130.4, 137.6, 140.5, 182.1, 208.3; MS: *m/z* 369; Anal. Calcd for $C_{19}H_{16}ClN_3O_3$: C, 61.71; H, 4.36; N, 11.36%; Found: C, 61.63; H, 4.24; N, 11.46%.

➢ *Spirooxindoles (CM-10)*

Yield: 66%; mp 283-285 ºC; IR (cm^{-1}): 3155 (=C-H str. of arg. ring), 2955, 2877 (C-H str. of alkane), 2119 (CN str. of cyanide), 1728 (C=O str. of carbonyl of ketone), 1681 (C=O str. of carbonyl of amide), 1604 (C=C str. of arg. ring), 1473, (C-H bending of alkane), 1219 (C-C str. of alkane), 1296 (C-O str. of ester), 1057, 1026(C-O-C str. of ester), 810 (C-H bending of *p*-di-substituted aromatic ring), 686, 624 (C-H bending of *o*-di-substituted aromatic ring), 645 (C-Cl str. of halogen); ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm: 0.827 (s, 6H, H_a), 0.97&1.00 (s, 4H, H_b), 2.11-2.51 (m, 3H, H_c), 3.36-3.73 (m, 2H, H_d), 6.65 (s, 1H, H_e), 7.01(d, 1H, H_f), 7.22(d, 1H, H_g), 7.95 (s, 2H, H_h), 10.33 (s, 1H, H_i); ^{13}C NMR (DMSO-d_6, 400 MHz) δ ppm: 14.1, 26.6, 30.4, 40.8, 44.2, 54.1, 60.8, 68.7, 111.3, 114.1, 127.9, 129.6, 130.4, 137.6, 140.5, 164.5, 182.1, 208.3; MS: *m/z* 416; Anal. Calcd for $C_{21}H_{21}ClN_2O_5$: C, 60.51; H, 5.08; N, 6.72%; Found: C, 60.43; H, 5.19; N, 6.83%.

Code	R	R_1	R_2	Molecular Formulas	Molecular Weights	Melting Points(ºC)	Yield (%)	R_f
CM-01	H	CN	CN	$C_{19}H_{17}N_3O_3$	335	273-275	82	0.56
CM-02	H	CN	COOEt	$C_{21}H_{22}N_2O_5$	382	268-270	78	0.52
CM-03	5-Br	CN	CN	$C_{19}H_{16}BrN_3O_3$	413	281-283	89	0.56
CM-04	5-Br	CN	COOEt	$C_{21}H_{21}BrN_2O_5$	460	271-273	76	0.54
CM-05	5-Cl	CN	CN	$C_{19}H_{16}ClN_3O_3$	369	275-277	84	0.53
CM-06	5-Cl	CN	COOEt	$C_{21}H_{21}ClN_2O_5$	416	272-274	75	0.52
CM-07	7-Br	CN	CN	$C_{19}H_{16}BrN_3O_3$	413	278-280	68	0.50
CM-08	7-Br	CN	COOEt	$C_{21}H_{21}BrN_2O_5$	460	269-271	67	0.54
CM-09	7-Cl	CN	CN	$C_{19}H_{16}ClN_3O_3$	369	286-288	68	0.63
CM-10	7-Cl	CN	COOEt	$C_{21}H_{21}ClN_2O_5$	416	283-285	66	0.61

Table 1: Physical data of (CM 01-10)

II. BIOLOGICAL ESTIMATION

➢ *Antimicrobial Estimation*

All the synthesized oxoindoline derivatives (Code- CM 01-10) were screened for their antibacterial and antifungal activities *in vitro* by broth dilution method[16-18] with two Gram-positive bacteria named *Staphylococcus aureus* MTCC-96, *Streptococcus pyogenes* MTCC-443, two Gram-negative bacteria named *Escherichia coli* MTCC-442, *Pseudomonas aeruginosa* MTCC-441 and three fungal strains named *Candida albicans* MTCC-227, *Aspergillus Niger* MTCC-282, *Aspergillus clavatus* MTCC-1323. The drugs which were used as standard drugs are ciprofloxacin, norfloxacin and nystatin. From the Microbial Type Culture Collection, Microcare Laboratory & Tuberculosis Research centre - Surat (India), the standard strains were procured.

The MIC i.e. Minimal or Minimum Inhibitory Concentration values for all the synthesized novel compounds were defined as the lowermost concentration of the compound which prevents the growth which is visible growth was calculated by using the micro-dilution broth method according to NCCLS standards. Sequential dilutions of the synthesized novel test compounds and standard reference drugs were produced in the Muellere-Hinton agar. Drugs (10.0 mg) were dissolved in DMSO i.e. Di-Methyl-Sulfoxide (1.0 mL). Progressive dilutions with melted Muellere-Hinton agar were carried out to obtain the required concentrations. In primary screening about 1000.0 µg mL^{-1}, 500.0 µg mL^{-1} and 250.0 µg mL^{-1} concentrations of the novel synthesized drugs were dissolved. Almost all the novel synthesized compounds found to be active in this primary screening and they were further tested in a second set of dilution at about 125.0 µg mL^{-1}, 100.0 µg mL^{-1}, 62.50 µg mL^{-1}, 50.0 µg mL^{-1}, 25.0 µg mL^{-1}, 12.50 µg mL^{-1} and 6.250 µg mL^{-1} concentration against all the microorganisms which were taken for the experiment. All the tubes before experiment were inoculated with 10.0^8 cfu mL^{-1} and incubated at the temperature around 38 ºC for about 24.0 hours. The MIC i.e. Mimimum or Minimal Inhibitory Concentration was actually the lowest concentration of the tested novel synthesized compounds which yield zero visible growth on the plate. To ensure that, the solvent had not at all any kind of effect on the bacterial growth, a control was calculated with the test medium supplemented with DMSO Di-Methyl-Sulfoxide solvent at the same dilutions which was used in the above experiments. It was observed that the solvent DMSO i.e. Di-Methyl-Sulfoxide has not at all any kind of effect on the taken microorganisms in the concentrations study. The practical result values obtained from above antimicrobial susceptibility experiment are showed in the following Table 2.

ISSN No:-2456-2165

Table 2:- Antibacterial activity as well as Antifungal activity of novel and synthesized derivatives (Code: CM 01-10)

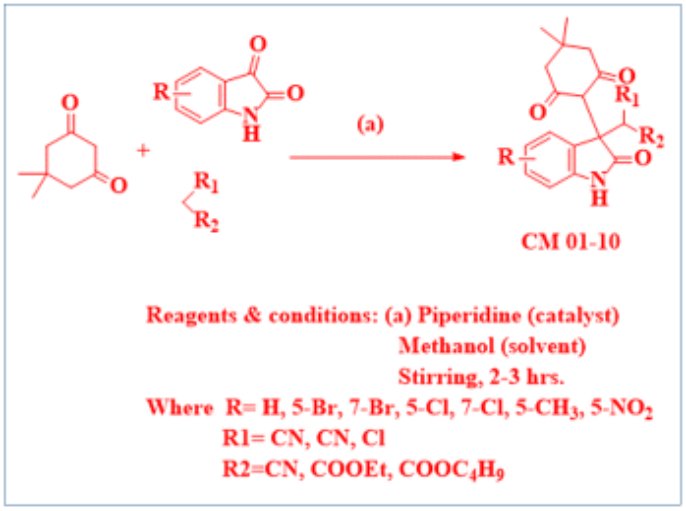
Code	MIC (Minimum Inhibitory Concentration Values (µg/mL)						
	Gram-positive Bacterias		Gram-negative Bacterias		Taken Fungal species		
	S.a.	***S. p.***	***E.c.***	***P.a.***	***C. a.***	***A. n.***	***A.c.***
CM-01	250	250	250	500	500	500	250
CM-02	500	500	250	250	500	250	250
CM-03	100	100	125	100	250	250	125
CM-04	100	62.5	100	100	250	250	100
CM-05	250	250	250	500	500	500	250
CM-06	500	500	250	250	500	500	500
CM-07	250	250	500	500	1000	500	500
CM-08	250	500	250	500	1000	500	500
CM-09	250	125	125	100	250	250	125
CM-10	100	100	125	250	250	500	500
Ciprofloxacin	25	25	12.5	12.5	-	-	-
Norfloxacin	12.5	12.5	12.5	12.5	-	-	-
Nystatin	-	-	-	-	50	50	50

III. MATERIAL AND METHODS:

The chemicals for research was bought from Merck and utilize in the synthesis. The reaction monitoring were carried out using thin-layer chromatography on precoated silica gel GF254 plates purchased E-Merck Co and visualized by under exposure of UV light. The m.p. was examined by open capillary method and are uncorrected. IR spectrums of synthesised compounds were examined using KBr pellet method on SHIMADZU-FTIR-8400 spectrophotometer. ^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker-Avance-II NMR spectrometer in DMSO-d_6 as a solvent. Tetramethylsilane used as reference slandered for chemical shift values. The Mass spectra were determined by using Shimadzu GCMS-QP 2010 mass spectrometer and C, H, N analysis was carried out using elemental analyser Heraus.

IV. RESULTS AND DISCUSSION

Recognizing these facts, here in we report one-pot synthesis of novel oxoindoline derivatives (CM 01-10) by three-component reaction of isatin or substituted isatin, substituted active methylene and dimedone in the presence of base as a piperidine. The mixture was stirred for 2-3 hour in methanol as solvent to give Spirooxindole derivatives. The final compounds was determined by FT-IR spectroscopy, Mass- spectrometry, ^{1}H NMR spectroscopy and ^{13}C NMR spectroscopy. The novel final synthesized compound was gives to various biological activities *viz.*, antibacterial & antifungal.



V. CONCLUSIONS

We report an atom-economical MCR reaction at ambient temperature by stirring in the presence of catalytic base as a piperidine along with methanol as a solvent to synthesize different oxoindoline derivatives CM-01 to CM-10. The results obtained from evaluation make them auspicious tools for additional *in vivo* and *in vitro* estimations for the development of lead with significant antimicrobial activity in the treatment of numerous dieses. Furthermore research and development are progress in our laboratory in this area.

ACKNOWLEDGEMENTS

This work was done by chemistry laboratory government Science College, veraval. I also wish to acknowledge Principal of government Science College, veraval, (Gir-Somnath) India for providing research facility.

REFERENCES

[1]. M.H. Chauhan, R.G. Vaghasiya, H.P. Parekh, V.H. Shah, vol. 3, Asian Jour. of Org. & Med. Chem., 2018, pp-139.
[2]. M.H. Chauhana, G.G. Dubal, V.H. Shah, vol. 4, Asian Jour. of Org. & Med. Chem., 2019, pp-201.
[3]. H.P. Parekh, M.H. Chauhan, N.L. Solanki, V.H. Shah, vol. 6, Asian Jour. of Org. & Med. Chem., 2021, pp-322.
[4]. M. Ona, K. Aoki, Chem. Abstr. 1989, pp-778–489.
[5]. J. W. Skiles, D. McNeil, vol. 31, *Tetrahedron Lett.* 1990, pp-7277.
[6]. H. Abdel-Rahman, E. M. Keshk, M. A. Hanna, S. M. El-Bady, vol. 12, Bioorg. Med. Chem., 2004, pp-2483–2488.
[7]. M. A. Koch, A. Schuffenhauer, M. Scheck, vol. 102, Proc. Natl. Acad. Sci. U.S.A., 2005, pp-17272–17277.
[8]. G. S. Singh, Z. Y. Desta, vol. 112, Chem. Rev., 2012, pp-6104–6155.
[9]. B. M. Trost, M. K. Brennan, vol. 18, Synthesis, 2009, pp-3003–3025.
[10]. N. R. Ball-Jones, J. J. Badillo, A. K. Franz, vol. 10, Org. Biomol. Chem., 2012, pp-5165–5181.
[11]. L. Hong, R. Wang, vol. 355, Adv. Synth. Catal., 2013, pp-1023–1030.
[12]. B. Tan, N. R. Candeias, C. F. Barbas, vol. 3, Nat. Chem., 2011, pp-473–4776.
[13]. F. Shi, S. W. Tao, S. J. Tu, L. Z. Gong, vol. 18, Chem. Eur. J., 2012, pp-6885–6894.
[14]. H. Deng, Y. Wei, M. Shi, vol. 13, Org. Lett. 2011, pp-3348–3351.
[15]. X. Peng, Y. Li, F. Li, vol.13,Org. Lett., 2011, pp-6160–6163.
[16]. K. Stratmann, R. E. Moore, R. Bonjouklian, J. B. Deeter, G. M. L. Patterson, S. Shaffer, C. D. Smith, C. A. J. Smitka, vol. 116, Am. Chem. Soc., 1994, pp-9935.
[17]. S. R. Yong, A. T. Ung, S. G. Pyne, B. W. Skelton, A. H. White, vol. 63, Tetrahedron, 2007, pp-1191.
[18]. E. M. Carreira, C. Meyers, vol. 42, Angew. Chem., Int. Ed., 2003, pp-694.