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ORIGINAL ARTICLE **OPEN ACCESS**

Synthesis of novel Amino Quinoline containing Schiff's bases and divalent Cu, Co, Ni and Zn metal complexes

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ABSTRACT

Reaction between Quinolin-7-amine (1) with aromatic various aldehydes (2a-j) according to the procedure depicted below. In a clean and dry round bottom flask, Quinolin-7-amine was dissolved in aqueous ethanol under continuous stirring on magnetic stirrer followed by slow addition of 30 cm3 of hot solution of aromatic aldehydes in EtOH. The above reaction mass was refluxed for 2 hrs on water bath. Schiff's base metal complexes were synthesized by adding of methanolic solution of 3a-j methanolic solution of metal (II) salts. The pH of reaction mass was maintained slightly basic by using 10% methanolic NaOH solution. It was refluxed for 2-3 hr. The reaction mass was concentrated to around and cooled at RT. The precipitated metal complexes were 4a-j containing Cu (II), Co (II), Ni (II), Zn(II) filtered out and washed with extra amount of MeOH.

Keywords: *Quinoline, aromatic aldehydes, Schiff's bases, bivalent metal complexes .*

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INTRODUCTION

Quinoline is one of the most frequently sustainable heterocyclic compounds in medicinal chemistry. Schiff's base has valuable uses in the field of medicinal chemistry, biology, analytical chemistry, organic and inorganic chemistry because their ability of complexation with different metals [1]. Based on this biological importance some of the quinoline moieties are used as drugs like chloroquine, Hydroxychloroquine, Quinacrine, Mefloquine, and Quinine.

It is well known fact that the presence of azomethine group (-C=N-) in Schiff's base make it more reliable in medicinal chemistry [2], because the presence of two electrons on -N atom, which actively participate in chelation with transition metal ions. Schiff's base compounds are well known to possess anti-bacterial [3-4], antitumor [5], anti-fungal [6-8], anti-cancer [9], anti-helminthics [10], anti-tuberculosis [11], DNA photo cleavage [12-15], DNA binding [16-19], analgesic [20], antioxidant [21] and anti-viral [22] properties.

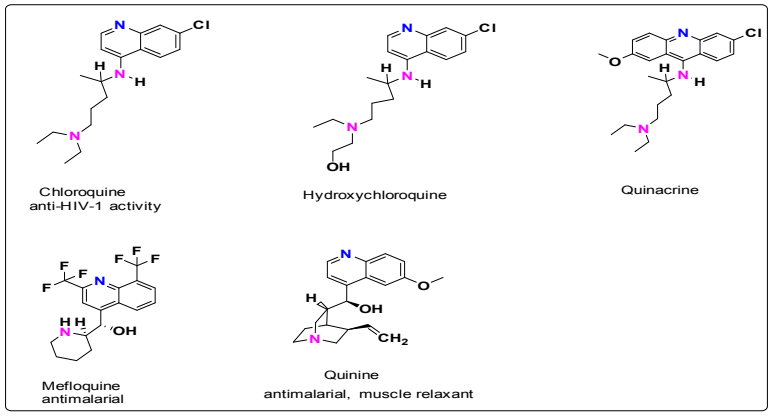


Figure 1. Quinoline Drugs

Herein we are going to synthesize the divalent quinoline based ligands and metal complexes depicted below (Figure 1 & 3)

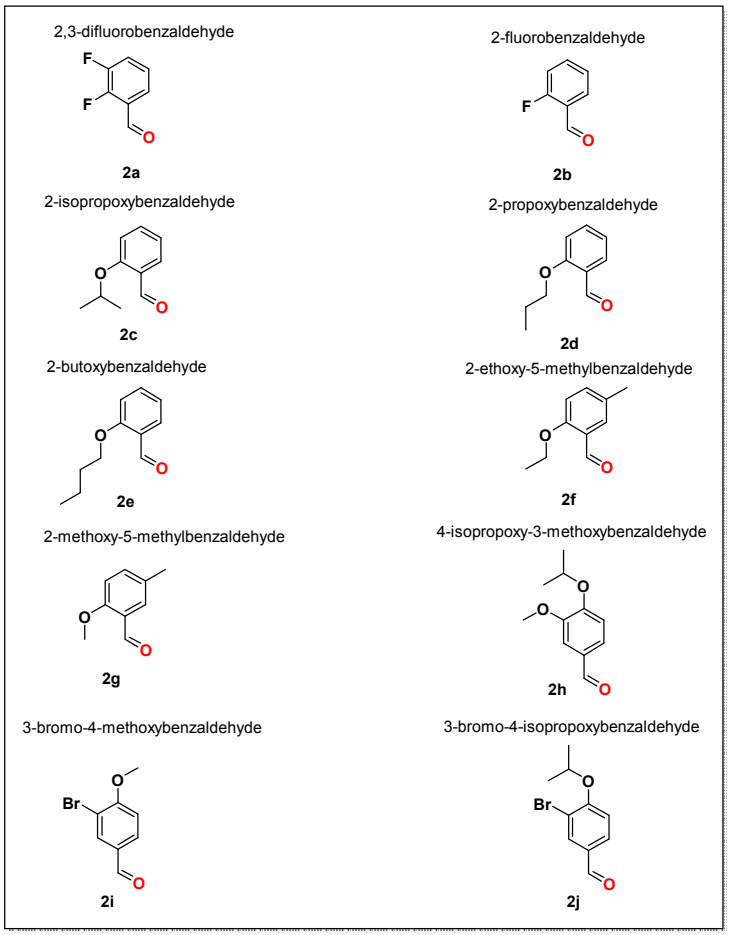
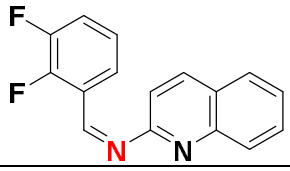
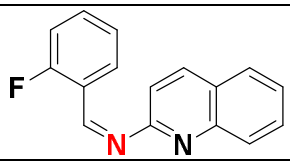
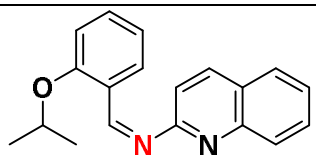
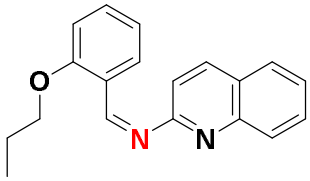


Figure-2: various ketones 2a-j

Entry	Name of the Schiff base with code	Structure
3a	(*Z*)-1-(2,3-difluorophenyl)- *N*-(quinolin-2-yl)methanimin DFPQMA	
3b	(*Z*)-1-(2-fluorophenyl)-*N*-(quinolin-2-yl)methanimin FPQMA	
3c	(*Z*)-1-(2-isopropoxyphenyl)-*N*-(quinolin-2-yl)methan IPFPQMA	
3d	(*Z*)-1-(2-propoxyphenyl)-*N*-(quinolin-2-yl)methanim PPQMA	

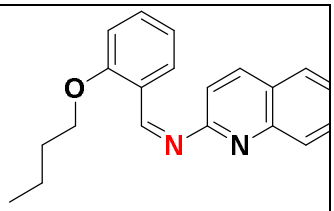
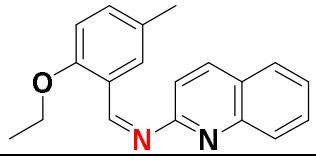
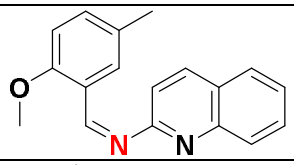
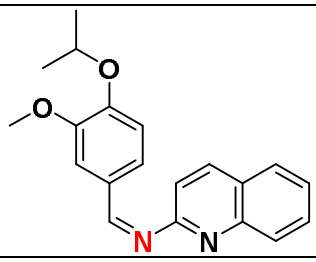
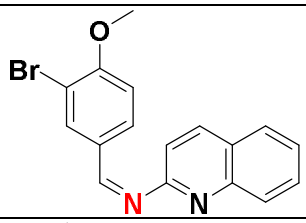
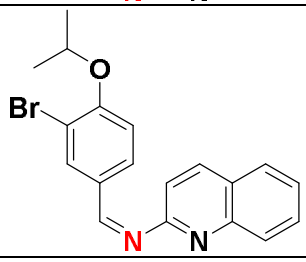
3e	(*Z*)-1-(2-butoxyphenyl)-*N*-(quinolin-2-yl)methanimi BPQMA	
3f	(*Z*)-1-(2-ethoxy-5-methylphenyl)-*N*-(quinolin-2-yl)m EMPQMA	
3g	(*Z*)-1-(2-methoxy-5-methylphenyl)-*N*-(quinolin-2-yl) MMPQMA	
3h	(Z)-1-(4-isopropoxy-3-methoxyphenyl)-N-(quinolin-2-yl)methanimine IPMPQMA	
3i	(*Z*)-1-(3-bromo-4-methoxyphenyl)-*N*-(quinolin-2-yl) BMPQMA	
3j	(*Z*)-1-(3-bromo-4-isopropoxyphenyl)-*N*-(quinolin-2- BIPPQMA	

Table 1: Schiff's bases 3a-j

Reaction between Quinolin-7-amine (1) with aromatic various aldehydes (2a-j) according to the procedure depicted below. In a clean and dry round bottom flask, Quinolin-7-amine was dissolved in aqueous ethanol under continuous stirring on magnetic stirrer followed by slow addition of 30 cm3 of hot solution of aromatic aldehydes in EtOH. The above reaction mass was refluxed for 2 hrs on water bath. Schiff's base metal complexes were synthesized by adding of methanolic solution of 3a-j methanolic solution of metal (II) salts. The pH of reaction mass was maintained slightly basic by using 10% methanolic NaOH solution. It was refluxed for 2-3 hr. The reaction mass was concentrated to around and cooled at RT. The precipitated metal complexes were 4a-j containing Cu (II), Co(II), Ni(II), Zn(II), filtered out and washed with extra amount of MeOH.

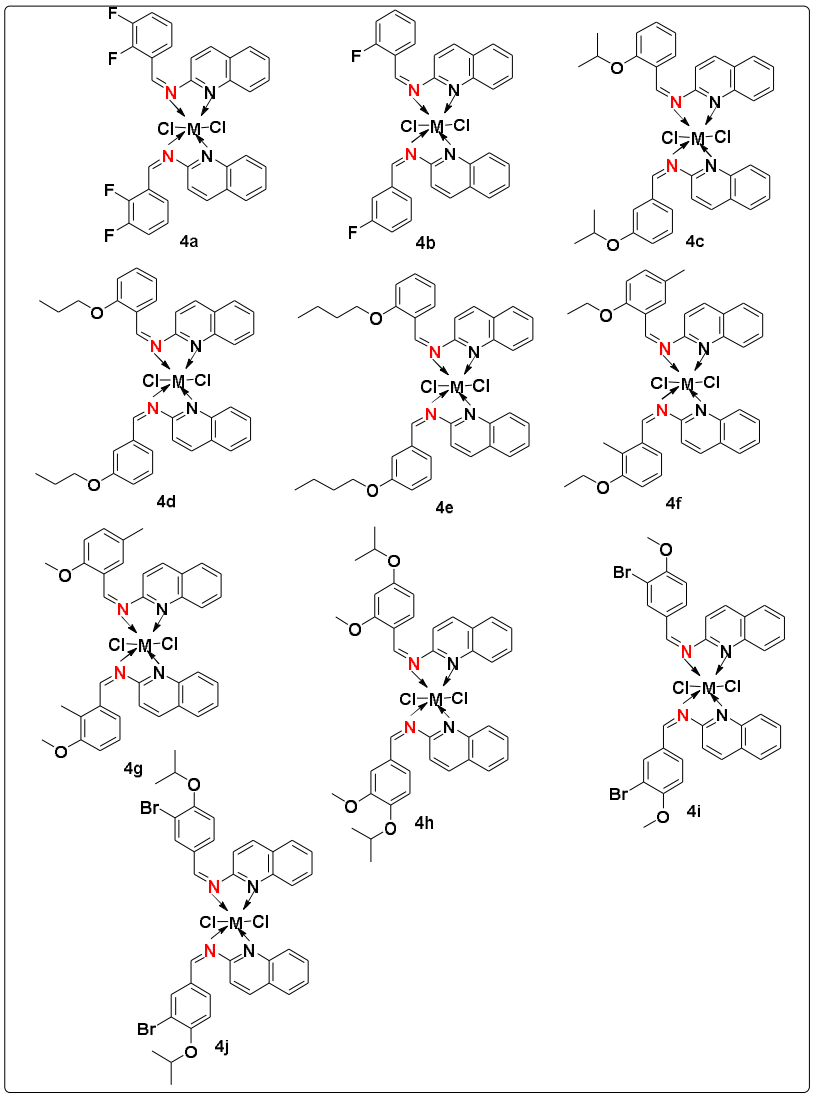
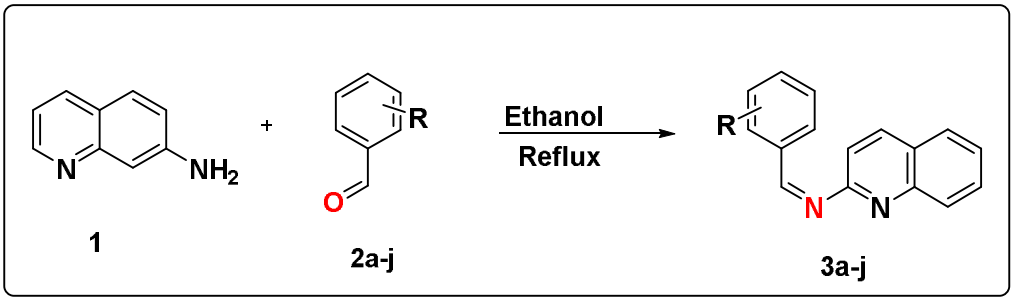
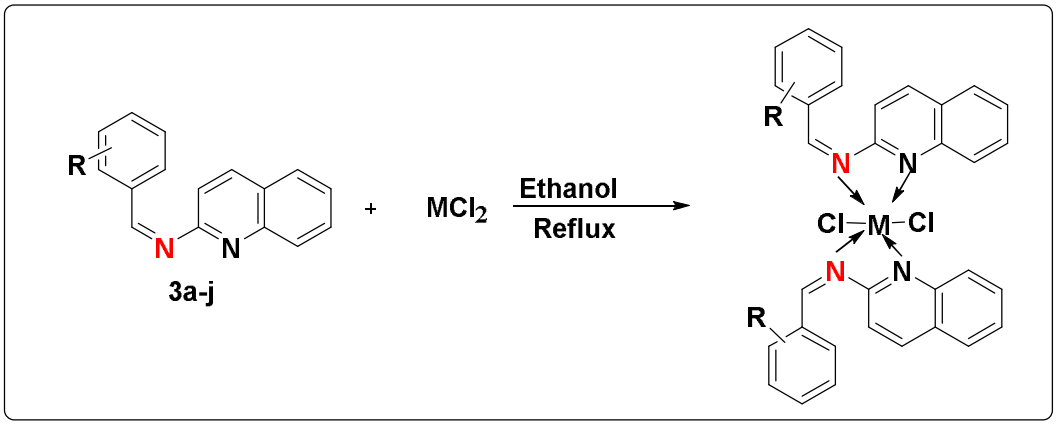


Figure-3: Metal complexes of Cu (II), Co (II), Ni (II) & Zn (II) 4a-j

RESULTS AND DISCUSSION



Scheme 1. Synthesis of Quinoline Schiff's bases (3a-j)



Scheme 2. Synthesis of Metal complexes (4a-j)

Synthesis of ligand 3a-j:

Quinolin-7-amine (1) (0.01 mol) with aromatic various aldehydes (2a-j) (0.01 mol) according to the procedure depicted below. In a clean and dry 100 cm3 round bottom flask, Quinolin-7-amine (0.02 mol) was dissolved in 30 cm3 aqueous ethanol (EtOH) under continuous stirring on magnetic stirrer followed by slow addition of 30 cm3 of hot solution of aromatic aldehydes (0.02 mol) in EtOH. The above reaction mass was refluxed for 2 hrs on water bath. The improvement of reaction was monitored with the help of thin layer chromatography (TLC). When reaction was completed cooled it to RT. Yellowish product formed was filtered and thoroughly washed with chilled EtOH. Product recrystalized from EtOH and dried in vacuum oven for 5-6 hrs at 55-60°C(Scheme-1).

Preparation of metal complexes [M(La)2Cl2] 4a-j:

The metal chloride salt (Cu, Co, Ni, and Zn) (0.1 mmol) and the synthesized Schiff base ligand (La) 3a-j (0.2 mmol) was dissolved in ethanol separately and mixed together (1:2 metal: ligand molar ratio). Then, the reaction mixture was heated under reflux for 6 h and colored precipitates were obtained. The resultant product was washed with ethanol, filtered and recrystallized. The obtained crystalline solid product was dried over anhydrous CaCl2 under vacuum condition.

Schiff's base metal complexes were synthesized by adding 40 cm3 of methanolic solution of 3a-j 10-15 cm3 methanolic solution of metal (II) salts. The pH of reaction mass was maintained slightly basic by using 10% methanolic NaOH solution. It was refluxed for 2-3 hr. The reaction mass was concentrated to around 30 cm3and cooled at RT. The precipitated metal complexes were filtered out and washed with extra amount of MeOH to get rid traces of unreacted metal salt; finally it washed with nonpolar solvent to get rid traces of unwanted impurities. Metal complexes were held in hot air oven at 65-70° C for 4-5 hr to remove moisture and solvents contents. Metal complexes were non hygroscopic and stable at RT(Scheme-2).

Table 2: **Mass data of the synthesized compound 4a-j**

Entry	Cu-complex		Co-complex		Ni-complex		Zn-complex	
	MF	m/z:	MF	m/z:	MF	m/z:	MF	m/z:
4a	C32H20Cl2CuF4N4	669.03	C32H20Cl2CoF4N4	652.03	C32H20Cl2NiF4N4	664.04	C32H20Cl2ZnF4N4	670.03
4b	C32H22Cl2CuF2N4	633.05	C32H22Cl2CoF2N4	629.05	C32H22Cl2NiF2N4	615.05	C32H22Cl2ZnF2N4	634.05
4c	C38H36Cl2CuN4O2	713.15	C38H36Cl2CoN4O2	709.15	C38H36Cl2NiN4O2	708.16	C38H36Cl2ZnN4O2	714.15
4d	C38H36Cl2CuN4O2	713.15	C38H36Cl2CoN4O2	709.15	C38H36Cl2NiN4O2	708.16	C38H36Cl2ZnN4O2	714.15
4e	C40H40Cl2CuN4O2	741.18	C40H40Cl2CoN4O2	724.18	C40H40Cl2NiN4O2	736.19	C40H40Cl2ZnN4O2	742.18
4f	C37H35Cl2CuN4O2	700.14	C37H35Cl2CoN4O2	709.15	C37H35Cl2NiN4O2	708.16	C37H35Cl2ZnN4O2	714.15
4g	C36H32Cl2CuN4O2	685.12	C36H32Cl2CoN4O2	681.12	C36H32Cl2NiN4O2	667.12	C36H32Cl2ZnN4O2	686.12
4h	C40H40Cl2CuN4O4	773.17	C40H40Cl2CoN4O4	769.18	C40H40Cl2NiN4O4	754.16	C40H40Cl2ZnN4O4	774.17
4i	C34H26Br2Cl2CuN4O2	814.91	C34H26Br2Cl2CoN4O2	810.91	C34H26Br2Cl2NiN4O2	809.91	C34H26Br2Cl2ZnN4O2	815.91
4j	C38H34Br2Cl2CuN4O2	870.97	C38H34Br2Cl2CoN4O2	866.97	C38H34Br2Cl2NiN4O2	865.98	C38H34Br2Cl2ZnN4O2	871.97

Chemistry

3a:MF: C16H10F2N2, 1H NMR (400 MHz, CDCl3) δ 8.20 (s, 4H), 8.09 – 7.97 (m, 8H), 7.71 (d, J = 8.9 Hz, 4H), 7.58 (td, J = 7.4, 1.5 Hz, 4H), 7.43 (dd, J = 7.4, 1.5 Hz, 3H), 7.28 – 7.07 (m, 16H).13CNMR (100MHz, CDCl3) δ 182.36, 163.60 , 163.60 , 165.54 , 151.15 , 145.77 , 134.71 , 130.49 , 127.90 126.20.LC-MS: m/z 268.08 [M]+.

3b: MF: C16H11FN2, 1H NMR (400 MHz, CDCl3) δ 8.15 (s, 1H), 8.06 (td, J = 7.2, 1.5 Hz, 2H), 7.71 (d, J = 7.5 Hz, 1H), 7.65 – 6.98 (m, 7H).13C NMR (100MHz, CDCl3) δ 182.19, 163.60 , 161.89 , 145.77, 135.28 , 134.71, 130.49, 127.91 , 127.07, 116.68.LC-MS: m/z 250.09 [M]+.

3c: MF: C19H18N2O6,1H NMR (400 MHz, CDCl3) δ 8.29 – 8.06 (m, 2H), 7.95 (dd, J = 7.4, 1.5 Hz, 1H), 7.72 (dt, J = 7.5, 1.4 Hz, 1H), 7.65 – 7.52 (m, 1H), 7.50 – 7.23 (m, 6H), 4.06 (d, J = 34.2 Hz, 1H), 1.35 (s, 6H).13C NMR (100MHz, CDCl3) δ 187.99, 163.60, 160.83, 145.77, 134.71, 134.06, 131.38, 130.49, 127.91, 127.07, 125.38 LC-MS: m/z 290.14[M]+.

3d: MF: C19H18N2O,1H NMR (400 MHz, CDCl3) δ 8.07 (dt, J = 8.6, 4.5 Hz, 3H), 7.80 – 7.69 (m, 1H), 7.58 (td, J = 7.5, 1.4 Hz, 1H), 7.49 – 7.20 (m, 3H), 7.16 – 6.76 (m, 3H), 3.97 (s, 2H), 1.87 (s, 2H), 1.01 (s, 3H).13C NMR (100MHz, CDCl3) δ 187.99, 163.60, 160.92, 145.77, 134.71, 133.22, 130.49, 127.07, 125.66, 125.38.LC-MS: m/z 290.14 [M]+.

3e: MF: C20H20N2O, 1H NMR (400 MHz, CDCl3) δ 8.07 (dd, J = 8.8, 6.1 Hz, 3H), 7.82 – 6.71 (m, 8H), 3.95 (s, 2H), 1.83 (s, 2H), 1.01 (s, 3H).13C NMR (100 MHz, CDCl3) δ 187.99 , 163.60 , 160.92 , 145.77 , 134.71 , 133.22 , 127.07, 123.81, 121.27.LC-MS: m/z 304.16 [M]+.

3f: MF: C19H18N2O,1H NMR (400 MHz, CDCl3) δ 8.24 – 7.89 (m, 3H), 7.79 – 7.50 (m, 2H), 7.38 – 7.20 (m, 2H), 6.98 (d, J = 7.0 Hz, 2H), 4.00 (s, 2H), 1.72 (s, 2H), 1.44 (s, 2H), 0.99 (s, 3H).13C NMR (100MHz, CDCl3) δ 187.40, 163.60, 156.40, 145.77, 134.71, 134.29 , 132.49, 131.02.LC-MS: m/z 290.16 [M]+.

3g: MF: C18H16N2O, 1H NMR (400 MHz, CDCl3) δ 8.31 – 7.97 (m, 3H), 7.79 – 7.23 (m, 4H), 7.15 – 6.80 (m, 3H), 3.82 (s, 3H), 2.27 (s, 3H).13C NMR (100MHz, CDCl3) δ 187.40, 163.60, 157.51, 145.77, 134.71, 134.49, 130.56, 116.25.LC-MS: m/z 276.13 [M]+.

3h: MF: C20H20N2O2,1H NMR (400 MHz, CDCl3) δ 8.36 – 7.95 (m, 3H), 7.79 – 7.28 (m, 4H), 7.22 – 6.78 (m, 3H), 4.06 (s, 1H), 3.72 (s, 3H), 1.41 (s, 6H).13C NMR (100MHz, CDCl3) δ 196.37, 163.60, 154.06, 145.77, 134.71,130.49, 127.07, 125.66, 125.38.LC-MS: m/z 320.15 [M]+.

3i: MF: C17H13BrN2O3,1H NMR (400 MHz, CDCl3) δ 8.05 (dd, J = 60.3, 19.2 Hz, 3H), 7.82 – 7.64 (m, 2H), 7.60 – 7.38 (m, 2H), 7.28 – 6.93 (m, 3H), 3.82 (s, 3H).13C NMR (100MHz, CDCl3) δ 196.37, 163.60 , 159.80 , 145.77, 132.67, 130.49, 129.31, 127.91, 126.07 .LC-MS: m/z 340.02 [M]+.

3j: MF: C19H17BrN2O, 1H NMR (400 MHz, CDCl3) δ 8.28 – 7.67 (m, 5H), 7.64 – 7.31 (m, 5H), 4.03 (d, J = 34.2 Hz, 1H), 1.46 (s, 6H).13C NMR (100MHz, CDCl3) δ 196.37, 163.60, 158.13, 145.77, 132.50, 129.48, 127.93, 127.07.LC-MS: m/z 368.05 [M]+.

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CONCLUSION

Herein we have synthesized active bivalent metal complexes containing quinoline moiety.

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