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NOVEL *N-O* TYPE OXAZOLINE LIGANDS

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We describe here the synthesis of three novel *N-O* type oxazoline compounds from readily available 3-hydroxy-2-naphthoic acid and pamoic acid (BINOL–box type) and 2-naphthol (Xabox type).

INTRODUCTION

Metal complexes of C_2-symmetry ligands have gained a reputation as efficient chiral catalysts in enantioselective catalytic transformations. In particular, chiral bisoxazolines (Box) have found broad use as chiral ligands due to their versatility and easy preparation. They have been used in a large number of asymmetric reactions. For instance, metal complexes of chiral bisoxazolines have been used in enantioselective cyclopropanation, allylic alkylation, Diels-Alder cycloaddition, oxidative addition reaction etc.[1-5] On the other hand, catalysis by dinuclear transition metal complexes of oxazoline ligands have the potential of catalyzing a reaction more efficiently or stereoselectively than mononuclear metal complexes. Mixed-metal systems offer the possibility for selective activation of two different reactants. Dinuclear metal complexes generally contain tetradentante nitrogen ligands.[6,7]

RESULTS AND DISCUSSION

We present herein some preliminary results on new types of mono and bisoxazoline ligands starting from 2-naphthol, 3-hydroxy-2-naphthoic acid and pamoic acid respectively (Figure 1). In order to synthesize compound **1**, 3-hydroxy-2-naphthoic acid was reacted with glyoxalaldehyde bisulfite in formic acid.[8] The carboxylic acid derivative was turned into acid chloride, and reacted with ethanolamine to get access to hydroxyamide compound that was cyclized in the presence of diethylaminosulfur trifluoride (DAST) to obtain bisoxazoline **1a** (Scheme 1).[9,10]

In the *cis*-7*a*,14*c*-dihydro-3,12-7,8-dioxa[6]helicene **1a** aromatic rings are not co-planar because interconversions of the enantiomers is observed in solution[11]. Compound **1a** can act as a chiral and tetradentate (*N-O-O-N*) or bidentate *N-O* ligand . The oxazoline rings are apart from each other which may allow the ligand to bind two metal atoms with each *N-O*. As mentioned before, this kind of dinuclear metal complexes have been a subject of great interest since there are examples in which dinuclear metal complexes catalyze the reactions more efficiently than the mononuclear ones.[6,7]

Bisoxazoline **2** was derived from pamoic acid and (*R*)-phenylglycinol. This BINOL-box type compound also has the possibility of combining two metal atoms like the ligand **1a.** However, in compound **2** chirality comes from oxazoline groups. Since phenolic salts have very poor solubility in organic solvents, in order to avoid potassium salt of the end product, we preffered Vorbrüggen method[12-14] (scheme 2) for synthesizing the compound **2.** By using Vorbrüggen method, it is possible to get oxazolines in one step reaction but, the large excess of triphenylphosphine that had to be used made

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isolation and purification of the product difficult. However, the suspensions of these salts in organic solvents may also be utilized to obtain oxazoline-metal complexes.

Compound **3** is a non-chiral N-O oxazoline ligand (Xabox-type)[14-16] derived from 2-naphthol and 2-(4-formyl phenoxy) acetic acid.[17,18] Chiral derivative of compound **3** can be prepared using chiral aminoalcohols. Different form the previously prepared xaboxes, in this compound oxazoline unit is not substituted on aromatic rings. There is an oxygen atom near the oxazoline unit which may allow the compound to act as a bidentate ligand. These type of ligands also use as catalyst 1,3-dipolar cycloaddition and Diels-Alder reactions.[15]

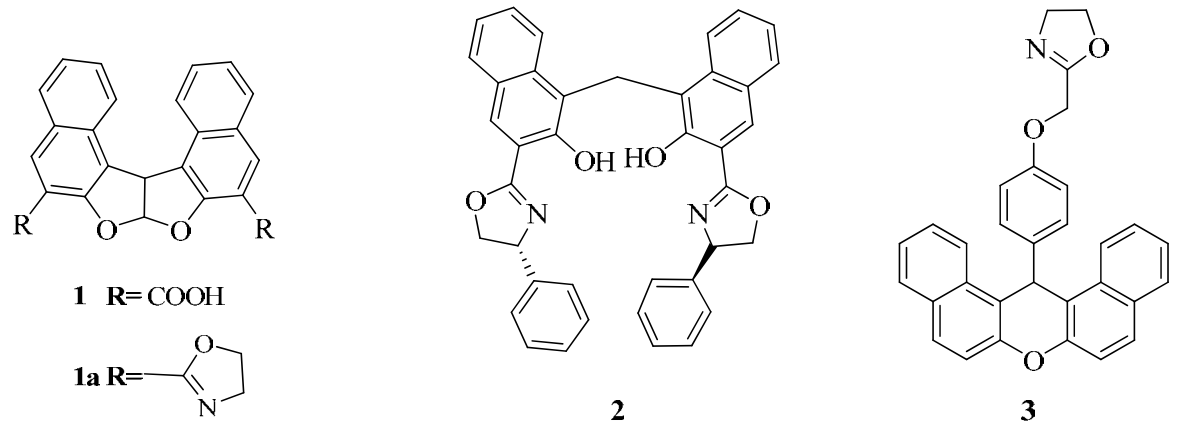
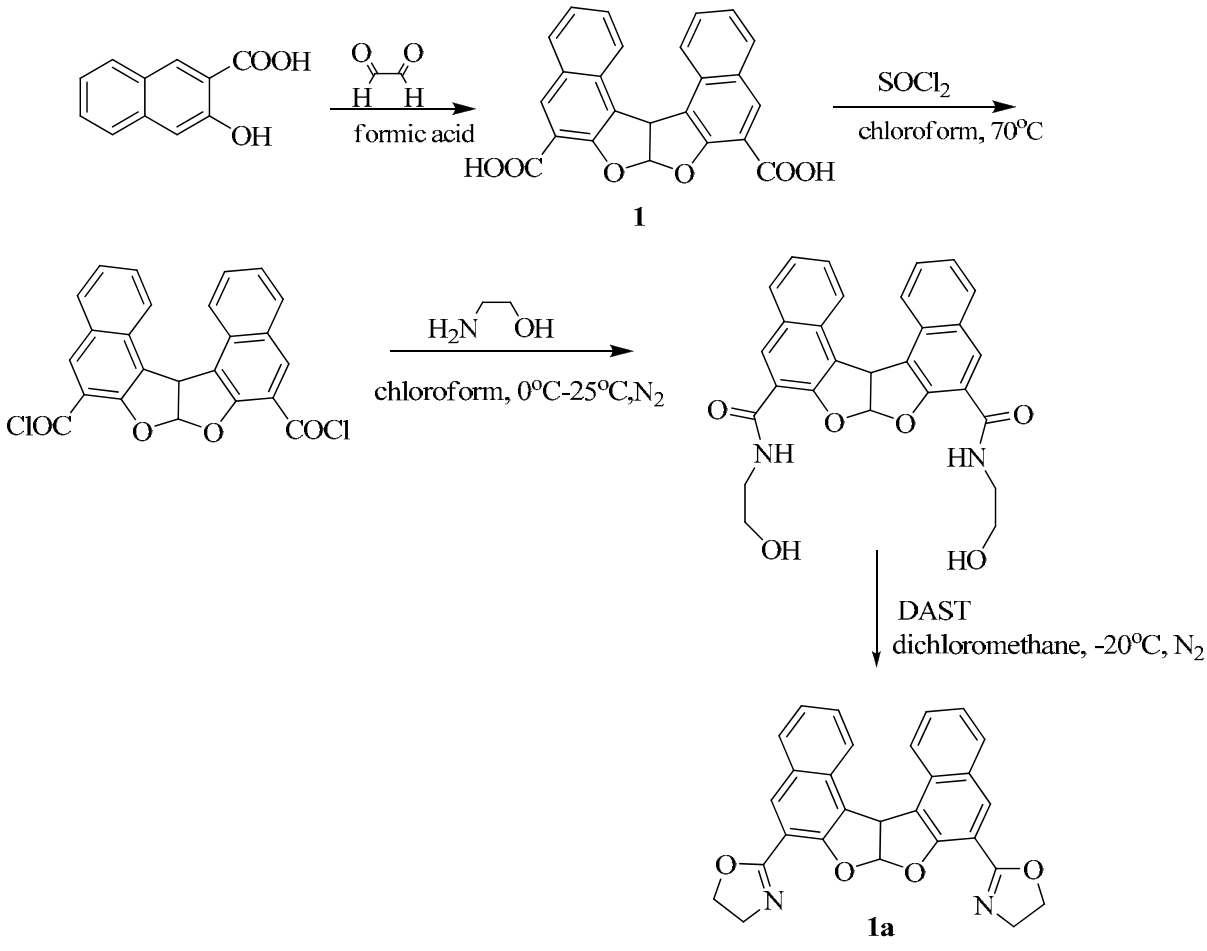
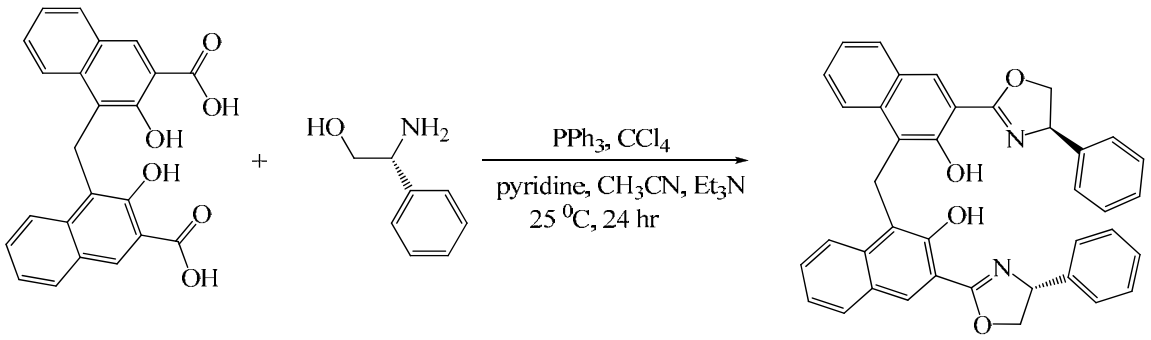


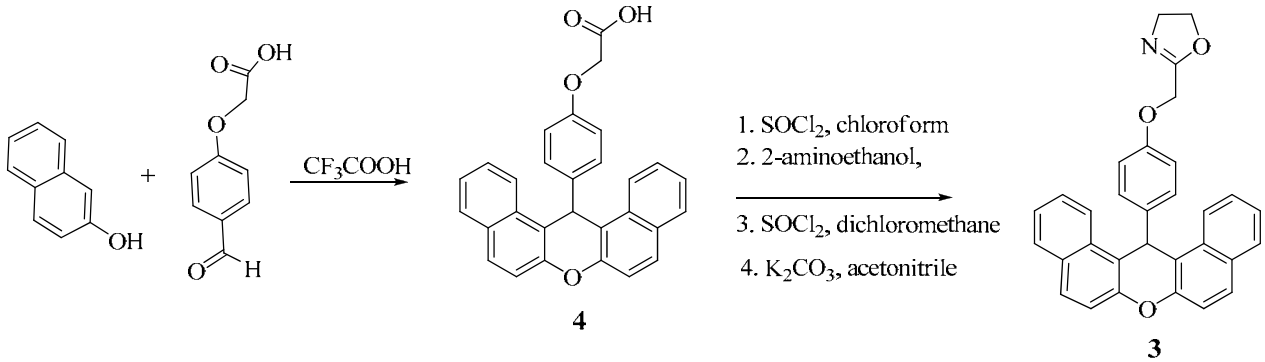
Fig. 1 – Synthesized ligand.



Scheme 1 – Reaction pathway for the synthesis of compound **1a**.



Scheme 2 – Reaction pathway for the synthesis of compound **2**.



Scheme 3 – Synthetic pathway of compound **3**.

In order to control the metal bonding structure of the ligands, zinc complex of ligands were prepared using $ZnCl_2$. From IR spectrum it was obsereved that ligand signal belonging to oxazoline C=N bond at 1658 cm^{-1} shifted to ~1637 cm^{-1}. From ^1H NMR oxazoline peaks were split and changed the chemical shifts.[21] However, exact structures of the metal complexes have not been determined yet.

EXPERIMENTAL

General Procedure. Melting points were determined by capillary tubes and are uncorrected. Fourier transform infrared (FT-IR) spectra were recorded on an Jasco FT-IR 5300 spectrometer. Absorption maxima were recorded in wave numbers (cm^{-1}). ^1H NMR and ^{13}C NMR spectra were recorded on Bruker AC-300 spectrometer. Residual non-deuterated solvent was used as internal reference and all chemical shifts (δ_H and δ_C) were quoted in parts per million (ppm) downfield from tetramethyl silane (TMS). Gas Chromatography mass spectrometer (GC MS) were recorded on a Thermo Finnigan Trace DSQ instrument using ZB-5MS capillary column. The products were purified by column chromatography on neutral silicagel 60 (0,040-0,063 mm) from Merck, Darmstadt. (*R*)-(-)Phenylglycinol$[\alpha]_D^{24}$= -31.7^0 was supplied from Aldrich.

6,9-Bis(4,5-dihydrooxazol-2-yl)-7a,14c-dihydro-naphtho[2,1-b]naphtho[1',2';4,5]-furo[3,2-d]furan (1a): 3-Hydroxy-2-naphthoic acid (0,94 g, 5 mmol) was dissolved in 15 mL formic acid and the temperature was raised to 60 ºC. After 2 h, 2,5 g glyoxalaldehyde bisulphite was added to the suspension, and the mixture was stirred overnight. Then, the reaction mixture was poured into water. The filtrate, compound **(1)**, was washed with water till neutralization and dried in open air. The off-white diacid product (0,60 g, 1,5 mmol, 30 %) was dissolved in 15 mL dry chloroform, thionylchloride (1,1 mL, 15 mmol) and 1 drop of DMF was added into the solution under nitrogen atmosphere. The reaction mixture was stirred at 68 ºC for 4 hours. After removing the heating source, diacid chloride precipitated. The greenish-white solid was collected via filtration, washed with chloroform, and dried in vacuum oven. Diacid chloride and freshly distilled 20 mL chloroform were put in a three-necked flask. The suspension was cooled to 0 ºC under nitrogen. Then a mixture of ethanolamine (0,09 g, 1,5 mmol) and triethylamine (0,1 mL, 1 mmol) in 10 mL of chloroform was added dropwise over 2 h. After 15 h of stirring, 10 mL of chloroform and ammonium chloride (1 g) was added. The suspension was stirred for extra 30 min, then filtrated, and washed 3 times with 20 mL of chloroform. The residue was solved in 25 mL of THF, stirred for 1 h, and filtrated. The combined organic phases were evaporated under reduced pressure. The residue was crystallized with methanol and white powder amidoalcohol was obtained. The amidoalcohol and 25 mL dichloromethane was added in a flask under nitrogen atmosphere, and cooled to -20 ºC. Diethylaminosulfur trifluoride (0,1 mL, 0,75 mmol) was added, and the suspension was stirred for 18 h at -20 ºC. Then, aqueous ammonium hydroxide (4 N, 1 mL) was added, and the reaction mixture was stirred for 15 min. After the removal of the cooling bath, 10 mL of water was added to the orange solution. The aqueous phase was extracted with dichloromethane (3 x 15 mL). The combined organic phases were evaporated under reduced pressure. The product was yellow powder. (0,42 g, the overall yield: 20 %) FTIR (KBr): 3395, 2952, 1718, 1648, 1520, 1458, 1365, 1276, 1260, 1214, 1158, 1063,1016, 982, 943, 906

cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 8.32 (s, 2H, Ar), 8.23 (d, *J=8.4* Hz, 2H, Ar), 7.83 (d, *J=8.0* Hz, 2H, Ar), 7.58 (t, *J=7.0* Hz, 2H, Ar), 7.40- 7.32 (m, 2H, Ar, 1H, CHO_2), 5.6 (d, *J=6.0* Hz, 1H, *CH*), 4.48 (t, *J=9.3* Hz, 2H, CH_2O), 4.20 (t, *J=9.2* Hz, 2H, CH_2N); Anal. Calcd. for $C_{28}H_{20}N_2O_4$; C, 74.99 ; H 4.50 ; N, 6.25. Found: C, 74.58 ; H 4.55 ; N, 6.28%.

3,3'-Bis((*R*)-4-phenyl-4,5-dihydrooxazole)-1,1'-methylenedinaphthalene-2,2'-ol (**2**): Pamoic acid (1,94g, 5 mmol) was dissolved in 25 mL pyridine and 25 mL acetonitrile mixture. Triethylamine (3,03 g, 0,06 mol), CCl_4 (0,125 mol) and (*R*)-(-)phenylglycinol (0,61 g, 0,01 mol) were added. Triphenylphosphine (0,786 g, 0,03 mol) was dissolved in 20 mL pyridine and 20 mL acetonitrile mixture, and added dropwise to the reaction mixture over 2 h. The reaction mixture was stirred 24 h at room temperature. Organic solvent was evoporated under reduced pressure, and the residue was dissolved in 50 mL of ethyl acetate, and washed with 20 mL of NH_4Cl solution. Then, organic phase was dried with sodium sulfate and evaporated. The crude yellowish brown product was chromatographed on silicagel (1:1 ethyl acetate/ toluene). Overall yield of pure product is 15%. FTIR (KBr): 3351, 3100, 2937, 1656, 1455, 1395, 1360, 1326, 1281, 1254, 1147, 1071, 1021, 986, 971, 950, 904, 844, 786, 761, 680 cm^{-1} ; ^{1}H NMR ($CDCl_3$): δ 4.36 (t, *J*=8,3 Hz, 2H, CH_2O), 4.88 (t, *J*=8,8 Hz, 2H, CH_2O), 5.03-5.59 (m, 2H, CH_2N), 5.59 (s, *J*=9.4 Hz, 2H, *benzylic*), 7.05-7.41 (m, 16H), 7.71 (d, *J*=8.1 Hz, 2H, Ar), 8.23 (s, 2H, Ar), 12.52 (s, 2H, ArOH). Anal. Calcd. for $C_{39}H_{30}N_2O_4$: C, 79.30; H, 5.12; N, 4.74. found: C, 78.51; H, 5.09; N, 4.52 %.

2-(4-(14*H*-Dibenzo[*a, j*]Xantene-14-yl)Phenoxy)Acetic Acid (4): 2-Naphthol (2,88 g, 20 mmol) was dissolved in10 mL trifloroacetic acid, and the temperature was raised to 60-65 ºC. Then, 0,1 mL methanesulphonic acid and 2-(4-formylphenoxy)acetic acid (1,8 g, 10 mmol, prepared from chloroacetic acid and 4-hydroxybenzaldehyde using potasium carbonate as catalyst, mp: 185 ^{0}C) was added to the solution, and the mixture was stirred for 18 h. The mixture was poured into the ice-cold water. The precipitate was filtrated, and washed with water. (Yield: 46 %, mp: 175 ºC) FTIR (KBr): 3079, 2930, 2500, 1734, 1645, 1592, 1225, 1216, 1076, 1076, 830, 805 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 4.45 (s, OCH_2), 6.67-6.65 (s, 1H, benzylic), 6.67 (d, H_7, H_{12}, *J*=8.4 Hz), 7.48 (d, phenyl, 2H, *J*=9 Hz), 7.55 (d, phenyl, 2H, *J*=9 Hz), (dd, H_3, H_{16}, *J*=7.4 Hz, *J*=8 Hz), 7.63 (dd, H_2, H_{17}, *J*=8.4 Hz, *J*=8 Hz), 7.91 (d, H_6, H_{13}, *J*=8.4 Hz), 7.93 (d, H_4, H_{15}, *J*=7.4 Hz), 8.66 (d, H_1, H_{18}, *J*=8.4 Hz).^{13}C NMR ($CDCl_3$) δ 40.9, 64.9, 114.6, 117.8, 123.5,124.6, 127.0, 128.7, 129.01 130.9, 131.1, 148.2, 156.3, 170.1.

2-(4-(14*H*-Dibenzo[*a,j*]Xantene-14-yl)Phenoxy)Methyl)-4,5-Dihydrooxazole (3): To the solution of 0,2 g 2-(4-(14*H*-Dibenzo[*a,j*]xantene-14-yl)phenoxy)acetic acid in 20 mL chloroform, was added 1,034 mL (8,69 mmol) thionyl chloride. The mixture was stirred at 68 ºC for 24 h. The excess thionyl chloride was evaporated under reduced pressure. The crude product was dissolved in 12 mL dichloromethane, and cooled to 0 ºC. In a second flask 0,062 mL ethanolamine (1,02 mmol) and 0,1 mL triethylamine (0,72 mmol) were dissolved in 10 mL of dichloromethane and cooled to 0 ºC. The content of the second flask was added dropwise to the reaction flask under argon atmosphere, and the resulting mixture was stirred 24 h at room temperature. Then, the mixture was cooled to 0 ºC. 0,44 mL (6,03 mmol) thionyl chloride in 4 mL dichlorometane was added to the reaction flask, and the mixture was stirred for 24 h. After addition of 10 mL of water, the organic phase was extracted 3 times with 15 mL of dichloromethane. Then, combined organic phases were washed 2 times with 10 mL of water, and evaporated under reduced pressure. To the crude solid product dissolved in 18 mL acetonitrile, was added 0,345 g potassium carbonate (2,5 mmol) dissolved in 4 mL of water, and the mixture was stirred 24 h at 95 ºC. After the evaporation of the solvents under reduced pressure, 10 mL water was added, and extracted three times with 20 mL of dichloromethane. The organic phase was washed with 1 M of HCl, and dried with sodium sulfate. After the removal of organic solvent under reduced pressure, the crude product was purified by preparative TLC by using 1/20; methanol/dichloromethane as eluent. (Yield: 40 %, mp: > 300 ºC). FTIR (KBr); 3100 $cm^{-1,}$ 2932 cm^{-1} , 1658 1645, 1592, 1239, 1177 1057, 964, 805 cm^{-1}.; ^{1}HNMR; 3.37 (t, -NCH_2, *J*=4.7 Hz), 3.59 (t, -OCH_2, *J*=4.7 Hz), 4.28 (s, -OCH_2), 6.43 (s, 1H, benzylic), 6.63 (d, phenyl, 2H, *J*=8.6 Hz), 7.42 (d, phenyl, 2H, *J*=8.6 Hz), 7.44 (dd, H_3, H_{16}, *J*=9.2 Hz, *J*=6.9 Hz), 7.46 (d, H_7, H_{12}, *J*=9 Hz), 7.56 (dd, H_2, H_{17}, *J*=8.5 Hz, *J*=6.9 Hz), 7.77 (d, H_6, H_{13}, *J*=9 Hz), 7.81 (d, H_4, H_{15}, *J*=9.2 Hz), 8.33 (d, H_1, H_{18}, *J*=8.5 Hz). ^{13}C NMR ($CDCl_3$) δ 43.8, 54.0, 68.2, 74.9, 114.8, 118.8, 123.2, 125.7, 127.03, 128.4, 129.1 130.8, 132.1, 148.2, 156.5, 166.8.
Anal.Calcd.for $C_{31}H_{23}NO_3$: C, 81.38; H, 5.07; N, 3.06. found: C, 81.57; H, 5.09; N, 3.02 %.

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