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Synthesis and characterization of some quinoline based bisphenols as sensing agents

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ABSTRACT

A series of potentially active quinoline based bisphenols has been synthesized by simple and efficient synthetic protocol. The quinoline based bisphenol, 4-((4-hydroxyphenyl)(quinolin-4-yl)methyl)phenol formed from quinoline-4-carbaldehyde and phenol in acetic acid medium followed by reaction with various substituted methyl groups. The newly synthesized bisphenols has an aromatic amine part which is fluorescence active and also can act as a binding site. The quinoline based bisphenols act as chemosensor when on addition of indium ion(+3), the curve is shifted towards the longer wavelength as well as the intensity of fluorescence emission spectra has been increased. The structure of the final analogues has been confirmed on the basis of ^{1}HNMR, IR and Mass analysis.

Keywords: Quinoline-4-carbaldehyde, bisphenol, fluorescence activity, chemosensor.

INTRODUCTION

Quinolines and their derivatives are important constituents of several pharmacologically active synthetic compounds[1-3]. They show biological activities such as DNA binding capability[4], antitumor[5], and DNA-intercalating carrier[6]. The quinoline based receptors are used for various metal ion detections. Especially the zinc ion sensitivity by quinoline based receptors is of great value[7-10]. Recently, they have been shown to be promising in anion recognition[11-12] and amino acid binding[13] In this work we are interested in coupling quinoline units to bisphenols, as bisphenols are organic compounds having propeller-like geometry, in which the phenolic hydroxyl groups play a critical role[14-15].

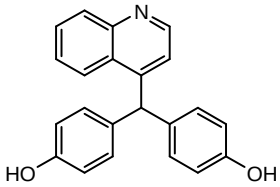


Figure 1: A quinoline functionalised bis-phenol

We have chosen quinoline based bisphenols for this study for the reason that it has an aromatic amine part which is fluorescence active and also can act as a binding site. Further the bisphenol part can self-assemble and be used in molecular recognition.

MATERIALS AND METHODS

Experimental: All the chemicals used in the synthesis were of analytical grade. The IR spectra (4000-400 cm^{-1}) of synthesized compounds were recorded on Perkin-Elmer FT-IR spectrophotometer with KBr pellets. Thin layer chromatography was performed on microscopic glass slides (2x7.5 cm) coated with silica gel-G, using appropriate

mobile phase system and spots were visualized under UV radiation. Nuclear magnetic resonance spectra were recorded on Varian 400 MHz model spectrometer using DMSO as a solvent and TMS as internal standard (Chemical shifts in δ ppm). All new compounds were subjected to elemental analysis and the results were in acceptable range.

Preparation of 4-((4-hydroxyphenyl)(quinolin-4-yl)methyl)phenol (1): A solution of quinoline-4-carbaldehyde (0.31g, 2mmol) and phenol (0.38g, 4mmol) in acetic acid (10ml) was stirred for half an hour in an ice bath. A mixture of concentrated sulphuric acid and glacial acetic acid in a 1:2 ratio (10 ml, v/v) was added dropwise to the reaction mixture. After half an hour, the mixture was kept in a deep freeze for one week. After one week, ice cold water (10ml) was added to the reaction mixture; a white precipitate appeared. The reaction mixture was filtered and the precipitate was washed with aqueous sodium bicarbonate solution (20%, 25 ml). A light yellow solid product was obtained. The crude product was purified by column chromatography by using hexane, ethylacetate as eluent (30%). **Yield:** 76% (calculated with respect to quinolin-4-carbaldehyde). **^{1}HNMR (400MHz, DMSO-d_6):** 9.36(d, 1H), 8.79(d, 1H), 8.1(d, 1H), 8.01(d, 1H), 7.7(t, 1H), 7.52(d, 1H), 6.89(d, 4H), 6.7(d, 4H), 6.19 (s, 1H). **FT-IR (KBr, cm^{-1}):** 3267 (b), 3022 (w), 1610 (m), 1511 (s), 1455 (w), 1384 (w), 1238 (m), 1112 (m), 837 (w), 755 (w). LC-**Mass:** [M+1]: 328.14

Preparation of 4-((4-hydroxy-3,5-dimethylphenyl)(quinolin-4-yl)methyl)-2,6- dimethylphenol (2): To a solution of quinoline-4-carbaldehyde (0.31g, 2mmol) and 2,6-dimethylphenol (0.49g, 4mmol) in acetic acid (10ml) placed in an ice bath, a mixture of concentrated sulphuric acid and glacial acetic acid in a 1:2 ratio (10ml, v/v). The mixture was kept in a deep freeze for one week. After one week, ice cold water (10ml) was added to the reaction mixture; a white precipitate appeared. The precipitate was washed with aqueous sodium bicarbonate solution (20%, 25ml). A light green coloured product is obtained. The crude product was purified by column chromatography by using hexane, ethylacetate as eluent (30%). **Yield:** 68% (calculated with respect to quinolin-4-carbaldehyde). **^{1}HNMR (400MHz, DMSO-d_6):** 8.78(d, 1H), 8.13(d, 1H), 8.01(d, 1H), 7.68(t, 1H), 7.51(t, 1H), 6.91(d, 1H), 6.64(s, 4H), 6.04(s, 1H),2.1(s, 12H),. **FT-IR (KBr, cm^{-1}):** 3412 (b), 2920 (w), 1637 (m), 1588 (m), 1488 (s), 1427 (w), 1385 (w), 1303 (w), 1200 (m), 1147 (m), 1024 (w), 871 (w), 854 (w), 756 (w). LC-**Mass:** [M+1]: 384.2

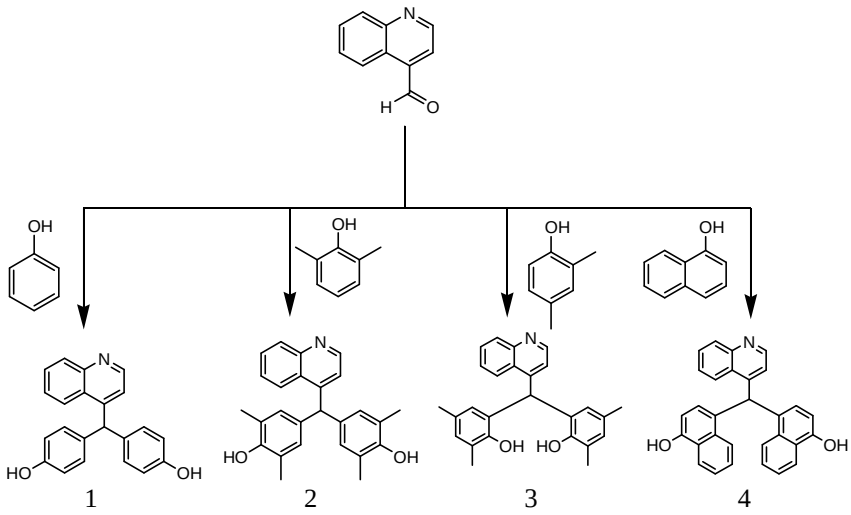
Preparation of 2-((2-hydroxy-3,5-dimethylphenyl)(quinolin-4-yl)methyl)-4,6- dimethylphenol (3): A mixture of concentrated sulphuric acid and glacial acetic acid in a 1:2 ratio (10 ml, v/v) was added dropwise to a solution of quinoline-4-carbaldehyde (0.31g, 2mmol) and 2,4-dimethyl phenol (0.49g, 4mmol) in acetic acid(10ml) and the solution was stirred for half an hour in an ice bath. After half an hour of stirring, the mixture was kept in a deep freeze for one week. After one week, ice cold water (10ml) was added to the reaction mixture; a white precipitate appeared. The reaction mixture was filtered and the precipitate was washed with aqueous sodium bicarbonate solution (20%, 25 ml). A light yellow coloured product is obtained. The crude product was purified by column chromatography by using hexane, ethylacetate as eluent (30%). **Yield:** 70% (calculated with respect to quinolin-4-carbaldehyde).**^{1}HNMR (400MHz, DMSO-d_6):** 8.97 (d, 1H), 8.75 (d, 1H), 8.19(s, 1H), 7.99(d, 1H), 7.68 (t, 1H), 7.52 (d, 1H), 6.78 (s, 4H), 6.32 (s, 1H), 2.14 (s, 12H). **FT-IR (KBr, cm^{-1}):** 3429 (bs), 2919 (w), 1637 (w), 1598 (m), 1483 (s), 1415 (m), 1199 (m), 1115 (s), 857 (m), 761 (m), 620 (m). **LC-Mass:** [M+1]: 384.18.

Preparation of 4-((1-hydroxynapthalen-4-yl)(quinolin-4-yl)methyl)napthalen-1-ol (4): The compound **4** was prepared in a similar procedure **1-3** but 1-naphthol (0.56g,4 mmol) was used as phenolic compound. **Yield:** 60% (calculated with respect to quinolin-4-carbaldehyde). **^{1}HNMR (400MHz, DMSO-d_6):** 8.7(d,1H), 8.21(d, 3H), 8.06(d, 3H), 7.97(d, 1H), 7.82(d,1H), 7.73(m, 4H), 7.47(d, 1H), 7.39(d, 2H), 6.74(d, 2H), 6.58(s, 1H). **FT-IR(KBr, cm^{-1}):** 3461(b), 3065 (w), 1659 (w), 1625 (w),1587 (s), 1449 (b), 385 (m), 1278 (m), 1212 (w), 1149 (w), 763 (s), 619 (w). **LC-Mass:** [M+1]:428.11

RESULTS AND DISCUSSION

Four different quinoline derivative of bisphenol compounds 1, 2, 3 and 4 were prepared by reacting quinoline-4-carbaldehyde with phenol, 2,6-dimethylphenol, 2,4-dimethylphenol and α-napthol respectively in the presence of acid. Bisphenols were formed in good yield as illustrated in scheme 1.

The compounds 1-4 were characterised by ^{1}HNMR, FT-IR spectroscopy and Mass spectrometry. As an illustrative case the ^{1}HNMR spectra of the compound 1 is shown in fig. 2. The compound has proton NMR peaks at 6.19 (s, 1H), 6.7(d, 4H), 6.89 (d, 4H), 7.52 (d, 1H), 7.7 (t, 1H), 8.01(d, 1H), 8.1(d, 1H), 8.79 (d, 1H), 9.36(d, 1H). The peak at 6.19 (s, 1H), is the characteristic methine hydrogen (Ha) peak which signifies the formation of disubstituted compound.



Scheme 1: The quinoline based bisphenols 1-4

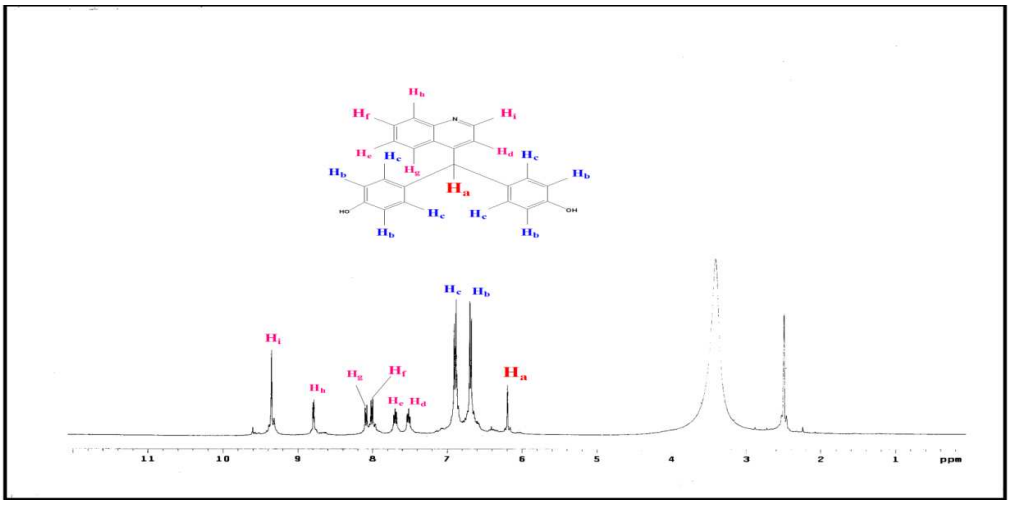


Figure 2: ^{1}HNMR (400MHz, DMSO-d_6) spectra of 1

The compound **1** is light yellow in colour and it is found that the absorption spectra come in the UV region. The spectra were recorded in different solvents such as DMSO, methanol, DMF, hexane and acetonitrile; but no significant change in wavelength is observed, only the intensity of absorption polar and non polar solvents are different. The absorption shows around 280 nm due to π-π* transition. The increase in absorption maximum with an increase in the polarity of the solvent implies that the energy necessary for the π-π* transition is less in more polar solvent due to stabilisation of the excited state by interaction with the solvent[16].

We have attempted synthesis of metal complexes of ligands, but it failed to get characterisable materials in pure form in such reactions. The binding study of ligand **1** with common transition metal ions e.g. Fe^{3+}, Ni^{2+}, Cu^{2+} etc. has been failed to change the UV-Visible spectra.

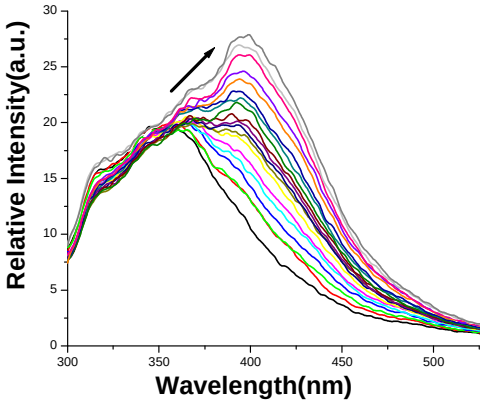


Figure: 3

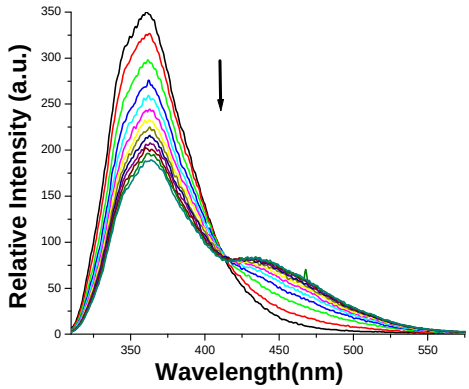


Figure: 4

Quinoline sensors, especially Zn^{2+} and Cd^{2+}, have high selectivity and low detection limit (nM or pM). Here the quinoline derivatives **1** shows an indium ion (+3) sensor when on addition of In^{3+} 10^{-3} M in methanol 10 µL in each aliquot as shown in fig. 3. It is observed that on addition of In3+ ion, the curve is shifted towards the longer wavelength as well as the intensity of fluorescence emission spectra has been increased. Photoinduced electron transfer (PET), intermolecular charge transfer (ICT) and fluorescence resonance energy transfer (FRET) are the three major mechanisms of fluorescence signal transduction in the design of quinoline based fluorescence chemosensors[17-18]. The quinoline derivative of bisphenol compound **1** has a fluorophore unit which shows fluorescence emission. On addition of different stereomeric acids, a significant change in fluorescence emission spectra has been observed. Fluorescence quenching of **1** solution by maleic acid shows a sharp decrease in intensity at 362 nm as shown in fig. 4. The quenching process is also observed in Fumeric acid but, change is too small. Fluorescence quenching provides the dynamic, resulting from collisional encounters between the fluorophore and the quencher, or static, resulting from the formation of a ground state complex between the fluorophore and the quencher[19]. The quinoline based chemosensor is used for various metal ion detection and it has been improved due to its easy synthesis, high sensitivity and stability[20]. The development of general methods for the synthesis and biological evaluation of new agents retaining the 'core' quinoline moiety is the subject of considerable synthetic effort. Certain small heterocyclic molecules act as highly functional scaffolds and are act as pharmacophores of a number of biologically active and medicinally useful molecules[21-25].

CONCLUSION

We have synthesized and characterized some quinoline based bisphenols. Quinoline nucleus is one of the active constituents present in many standard drugs, and is known to increase in pharmacological activity of the molecules. we cover quinoline-based chemosensors for detection of indium(+3) metal ion. There has been tremendous interest in improving quinoline-based chemosensors due to its easy synthesis method, high sensitivity and stability. However, there is still much room for progress in its application in vivo such as water solubility, high selectivity, and fluorescence bio-imaging capacity.

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