Synthesis and characterization of new fatty Schiff base ethers of 4-((pyridin-3-ylmethylimino)methyl)phenol

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1. Introduction

Schiff bases are compounds containing imine or azomethine moiety, a nitrogen analogue of an aldehyde or a ketone, where the carbonyl group (C=O) is replaced by an imine (or) azomethine group. Schiff bases are organic compounds used as pigments and dyes, catalysts, intermediates in organic synthesis and as polymer stabilizers [1]. The azomethine group present in the molecules exhibits many biological activities [2-4]. Literature survey revealed that, most of the Schiff bases exhibit wide range of biological activities like anti-fungal, anti-bacterial, anti-malarial, anti-inflammatory and antipyretic properties [5-10]. Similarly, fatty acids and derivatives showed biological activities like antimicrobial [11,12], antifungal [13], and pesticidal activities [14] and the presence of ether bond linked to a lipid molecule further increases the biological activity [15]. The existence of ether bond increases the resistance of a molecule to hydrolysis and forms chemically stable bond. Keeping this in view, in the present study, we focussed on the synthesis of a homologous series of ten novel Schiff base ethers by the etherification of Schiff base-4-((pyridin-3-ylmethylimino)methyl)phenol.

2. Experimental

2.1. Instrumentation

Schiff base (1) (4-(pyridine-3-methylimino) methyl phenol) was prepared by the condensation of 4-hydroxy benzaldehyde (2 mmol) and 3-aminomethyl pyridine (2 mmol) in absolute ethanol for 6 h at 80-85 °C [Scheme 1] which yielded Schiff base [16]. C18H13N3O. Yield: 80%. M.p.: 143.6 °C. 1H NMR (300 MHz, DMSO-d6, δ, ppm): 4.72 (s, 2H, N-C=), 6.79 (J, Ar-H), 7.69 (d, 2H, J = 8.4 Hz, Ar-H), 7.26 (d, 2H, J = 8.3 Hz, Ar-H), 7.57 (d, 2H, J = 7.7 Hz, Ar-H), 7.66 (d, 1H, J = 3.5 Hz, Ar-H), 7.30 (s, 1H, Ar-H), 8.32 (d, 1H, J = 4.7 Hz, Ar-H), 8.52 (s, 1H, CH=N), 9.6 (s, 1H, Ar-H).

3H and 13C NMR spectra were recorded on AVANCE 300 and 500 MHz and 75 MHz, respectively in CDCl3 and DMSO-d6. Chemical shifts relative to TMS as internal standards were given as δ values in ppm while the coupling constants were measured in Hz values. The melting point was determined through open capillary tubes which are uncorrected. Infrared (IR) spectra were obtained on a 1600 FT-IR Perkin-Elmer Spectrometer (Norwalk, CT) with a liquid film between NaCl cells. Mass spectrometry was recorded by electron spray ionization (ESI) on Shimadzu LC/MS instrument.

2.2. General procedure for the synthesis of Schiff base 4-((pyridine-3-ylmethylimino)methyl)phenol (1)

Schiff base (1) (4-(pyridine-3-methylimino) methyl phenol) was prepared by the condensation of 4-hydroxy benzaldehyde and 3-aminomethyl pyridine in absolute ethanol for 6 h at 80-85 °C.

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2.2. Typical procedure for the synthesis of compound 2a-j

N-(4-butoxybenzylidene)-1-(pyridin-3-yl)methanamine was synthesized by etherification of Schiff base 1 with 1-bromo butane taken in equimolar ratios (Scheme 1). A solution of Schiff base (0.40 g, 2 mmol) and 1-bromo butane (0.27 g, 2 mmol) and little excess amount of base, potassium carbonate (2.76 g, 10 mmol) was dissolved in 50 mL dry acetone under N₂ atmosphere and the contents were refluxed for 12 h stirring magnetically. The progress of the reaction was monitored using thin layer chromatography eluted with the solvent CHCl₃/MeOH (95:5, v.v.). The reaction was cooled to 45 °C, filtered off the by-product and washed with 20 mL dry acetone. The acetonitrile was filtered, dissolved in ethyl acetate and the crude product was extracted with hexane and acetonitrile, where the pure product went into the hexane layer. The hexane layer was concentrated to yield N-(4-butoxybenzylidene)-1-(pyridin-3-yl)methanamine.

Similarly all the Schiff base ethers, (4-allyloxybenzylidene)-pyridin-3-ylmethyl amine (2b-j) were prepared following the above procedure (Scheme 1). The synthesized Schiff base ethers were characterized by FT-IR, ¹³C NMR and Mass spectral studies.

N-(4-Butoxybenzylidene)-1-(pyridin-3-yl)methanamine (2a):

Yield: 80% (C₁₉H₂₂N₂O). FT-IR (vmax, cm⁻¹): 2980 (C-H aliphatic), 1625 (C=N), 1510 (C-O), 1039 (C-O). ¹³C NMR (300 MHz, CDCl₃, δ, ppm): 140.05, 148.21, 149.31, 161.55 (Aromatic carbons), 162.08 (‐C=C=CH₂). MS/ESI (m/z): 268 [M+1], 269 [M+2].

N-(4-(Hexyl)benzylidene)-1-(pyridin-3-yl)methanamine (2c):

Yield: 80% (C₁₇H₂₄N₂O). FT-IR (vmax, cm⁻¹): 2980 (C-H aliphatic), 1610 (C=N), 1587 (C=C), 1039 (C-O). ¹³C NMR (300 MHz, CDCl₃, δ, ppm): 140.05, 148.21, 149.31, 161.55 (Aromatic carbons), 162.08 (‐C=C=CH₂). MS/ESI (m/z): 311 [M+1], 312 [M+2].

N-(4-(Octyl)benzylidene)-1-(pyridin-3-yl)methanamine (2d):

Yield: 85% (C₁₉H₂₄N₂O). FT-IR (vmax, cm⁻¹): 2980 (C-H aliphatic), 1625 (C=N), 1539 (C=C), 1040 (C-O). ¹³C NMR (300 MHz, CDCl₃, δ, ppm): 140.05, 148.21, 149.31, 161.55 (Aromatic carbons), 162.08 (‐C=C=CH₂). MS/ESI (m/z): 314 [M+1], 315 [M+2].

Scheme 1

R = butyl (2a), pentyl (2b), hexyl (2c), heptyl (2d), octyl (2e), decyl (2f), dodecyl (2g), tetradecyl (2h), hexadecyl (2i), octadecyl (2j)

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CH-(CH2)-1.79 (quint., 2H, -CH2-CH2-), 3.99 (t, 2H, J = 6.6 Hz, -CH2-O), 4.78 (s, 2H, -CH2-N=CH), 6.92 (d, 2H, J = 9.0 Hz, Ar-H), 7.28 (d, 1H, J = 6.8 Hz, Ar-H), 7.67 (d, 1H, J = 8.0 Hz, Ar-H), 7.71 (d, 2H, J = 8.9 Hz, Ar-H), 8.35 (s, 1H, Ar-H), 8.51 (dd, 1H, J = 4.0 Hz, Ar-H), 8.60 (s, 1H, -CH=N), 13.05, 30.24, 31.56, 32.85 (Methylene carbons), 61.15 (-CH-N=CH-), 114.50, 122.39, 129.67, 132.32, 134.50, 138.57, 140.23, 149.19, 161.12 (Aromatic carbons), 162.04 (-C=O-N=CH-).

N-(4-Hexadecyloxy)benzylidene)1-(pyridin-3-yl)methanamine (2b): Yield: 68% (C6H14N2O). FT-IR (v max, cm⁻¹): 2895 (C=H aliphatic), 1620 (C=N), 1520 (C=O), 1039 (C-O). 1H NMR (300 MHz, CDCl3, δ, ppm): 0.88 (t, 3H, J = 7.0 Hz, -CH3), 1.26 (m, 26H, -CH2-CH2-), 1.78 (quint., 2H, -CH2-CH2-), 3.98 (t, 2H, J = 6.6 Hz, -CH2-O), 4.78 (s, 2H, -CH2-N=CH), 6.92 (d, 2H, J = 8.6 Hz, Ar-H), 7.29 (d, 1H, J = 6.5 Hz, Ar-H), 8.61 (d, 1H, J = 8.6 Hz, Ar-H), 8.51 (dd, 1H, J = 4.5 Hz, Ar-H), 8.50 (s, 1H, Ar-H), 8.60 (s, 1H, -CH=N), 13.05, 30.24, 31.56, 32.85 (Methylene carbons), 61.05 (-CH=N=CH-), 114.50, 122.40, 129.70, 132.66, 135.23, 138.61, 148.04, 149.22, 161.02 (Aromatic carbons), 161.24 (-C=O-N=CH-).

N-(4-Octadecyloxy)benzylidene)1-(pyridin-3-yl)methanamine (2j): Yield: 80% (C6H14N2O). FT-IR (v max, cm⁻¹): 2890 (C=H aliphatic), 1621 (C=N), 1540 (C=O), 1040 (C-O). 1H NMR (300 MHz, CDCl3, δ, ppm): 0.88 (t, 3H, J = 6.7 Hz, -CH3), 1.27 (m, 26H, -CH2-CH2-), 1.78 (quint., 2H, -CH2-CH2-), 3.98 (t, 2H, J = 6.6 Hz, -CH2-O), 4.78 (s, 2H, -CH2-N=CH), 6.92 (d, 2H, J = 8.6 Hz, Ar-H), 7.29 (d, 1H, J = 6.5 Hz, Ar-H), 8.61 (d, 1H, J = 8.6 Hz, Ar-H), 8.51 (dd, 1H, J = 4.5 Hz, Ar-H), 8.50 (s, 1H, Ar-H), 8.60 (s, 1H, -CH=N), 13.05, 30.24, 31.56, 32.85 (Methylene carbons), 61.05 (-CH=N=CH-), 114.52, 123.36, 129.82, 131.99, 135.14, 134.64, 148.11, 149.23, 161.50 (Aromatic carbons), 162.12 (-C=O-N=CH-).

3. Results and discussion

Etherification was carried out by the reaction of Schiff base with fatty alkylation bromides of different chain lengths in the presence of base like potassium carbonate. Different fatty alkylation bromides employed were butyl (C4), pentyl (C5), hexyl (C6), heptyl (C7), octyl (C8), decyl (C10), tetradecyl (C14), hexadecyl (C16), octadecyl (C18) bromides. The structure of the Schiff base ethers was confirmed by FT-IR, 1H NMR, 13C NMR and Mass Spectral Studies. These synthesized compounds will be evaluated for biological properties as an extension to the presence of work and the influence of different chain lengths along the activity will be studied. The synthesis of different Schiff base ethers was carried out using the following procedure.

Schiff base was prepared by a mixture of equimolar quantities of 4-hydroxy benzaldehyde with 3-aminomethyl pyridine in absolute ethanol under reflux to give the corresponding Schiff base [16]. The 1H NMR spectra of Schiff base showed a signal at 8.5-8.6 ppm which confirmed the proton indicating the presence of azomethine group (-CH=N). The Schiff base (1) was etherified with different fatty alkylation bromides to give the corresponding Schiff base ethers (2a-j) that was indicated by the presence of a triplet at 3.96-4.01 ppm in 1H NMR spectra. The synthesised Schiff base ethers were also characterized by FT-IR which showed the presence of C-O stretching frequency at 1039 cm⁻¹. Mass spectra of the synthesized Schiff base ethers showed characteristic molecular ions as indicated by their molecular formulae.