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Spectroscopic Elucidation And DNA Binding Evaluation Of Molybdenum (VI) With 4-Methyl (Methoxy)Benzaldehyde Semicarbazone.

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ABSTRACT

In mole ratio 1:2, six molybdenum (VI) complexes were synthesized by the reaction of $MoO_2(acac)_2$ with semicarbazone ligands derived from 4-methylbenzaldehyde (1A and 2A), and 4-methoxybenzaldehyde (1B and 2B). The synthesized ligands and complexes were structurally characterized by CHNS elemental analysis and FTIR, ^{1}HNMR and ^{13}CNMR spectroscopic techniques. The DNA binding activity with all the compounds was investigated using the spectral titration method and the viscosity measurement. The results revealed the external groove binding mode of the ligands 2A, 1B and 2B, and all the complexes with DNA while, the ligand 1A showed an intercalation binding with DNA. The calculated binding constants (K_b) were extracted and the values exhibited a noticed binding strength with DNA.

Keywords: Semicarbazone, Groove DNA binding, UV titration, Binding constant, Viscosity

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INTRODUCTION

The synthesis and characterization of oxygen, sulfur and nitrogen donor ligands have received special interest in coordination chemistry. Among of interesting ligands are semicarbazones and thiosemicarbazones due to their variable binding modes, structural variety and biological applications [1-3]. Metal ions bind are provide flexibility to these ligands which are can be coordinated in mono- or poly-nuclear complexes [4-7]. Furthermore, semicarbazone and thiosemicarbazone complexes show typical stability, causing to boosting the biological activity, reduced toxicities and become a reliable source for discovering novel biologically active compounds [8, 9].

Molybdenum is one of the essential elements distributed in biological systems [10]. The biological form of Mo present in approximately all Mo-containing enzymes (molybdoenzymes) is bound to a unique tricyclic pterin compound known as the molybdenum cofactor (Moco). In human, molybdoenzymes are classified according to the structural homology of their active sites into three families. The first family includes xanthine oxidase, which has a monooxomolybdenum core. This enzyme catalyzes the hydroxylation of carbon centers and the breakdown of nucleotides to form uric acid. The second family includes sulfite oxidase, which has a dioxomolybdenum core. This enzyme, an important molybdoenzyme in human, catalyzes the transformation of sulfite to sulfate, a necessary reaction for sulfur-containing amino acid metabolism. Deficiencies of this enzyme have been reported in human and are usually fatal in infancy. The third family includes dimethyl sulfoxide (DMSO) reductase, with two equivalents of pterin cofactor bound to mono-oxomolybdenum [11].

DNA plays an important role in the biological processes due to its role in carrying the inheritance information and directed the biological synthesis of proteins and enzymes during the replication and transcription of genetic information in living cells [12]. The molecular interaction of the transition metal complexes and DNA has received increasing interest in recent years because of its importance in the design and development of the chemotherapeutic drugs. This interaction is important for understanding the molecular mechanism of drug action for designing a specific DNA targeted drug [13, 14]. The natural and synthetic products or the derivatives of low molecular weight molecules recognize DNA and interact with it via specific ways. The DNA interaction with small molecules was received an active research in field of chemistry and biology [15-18]. These molecules are stabilize into DNA during binding through non-covalent interactions, such as the π stacking interactions associated with interacting between the base pairs of nitrogenous bases, Van der Waals interactions of functionalities bound along the groove of the DNA helix [19], and the electrostatic interaction of the cation with the phosphate group of DNA [20]. Transition metal complexes bind to DNA provide attractive applications such as new cancer therapeutic agents, potential artificial gene regulators, or probes of DNA structure and conformation [21].

Dioxomolybdenum (VI) complexes with tridentate donor ligands have attracted substantial attention as model systems for molybdoenzyme active site, which Mo exhibits a normal octahedral geometry [22]. In this work, we describe the synthesis, characterization and DNA binding of dioxomolybdenum (VI) complexes based on semicarbazone derivatives ligands and investigates their interaction activity with DNA. The synthetic routes for the ligands and their corresponding Mo(VI) complexes are shown in Scheme 1.

EXPERIMENTAL

Materials and instrumentation

All chemicals were purchased from Sigma Aldrich/Merck, and used without more purification. DNA obtained from human blood. Melting points were measured using BCUI 510 melting point apparatus. FTIR spectra were recorded on a Shimadzu (FTIR-8400S, Japan) spectrometer using KBr pellets. Electronic spectra were recorded on a UV-Vis double-beam spectrophotometer using cuvettes of 1 cm path length (Spectroscan-80D, England). ^{1}HNMR and ^{13}CNMR spectra were recorded on a BRUKER 400 MHz spectrometer using DMSO-d_6 as solvent. Elemental analysis was performed on Eager 300 CHN analyzer.

DNA binding assay

The binding with human DNA were performed in 6.3 mM Tris-HCl/50 mM NaCl buffer (pH = 7.2). DNA stock solution was prepared by dissolving a suitable amount of DNA in buffer solution (1 ml) at room temperature and stored in refrigerator. DNA stock concentration was estimated by the UV absorbance at 260 nm using the known molar absorption coefficient of 6600 M^{-1} cm^{-1} [23]. The absorption titrations were performed using a known concentration of the ligands or complexes (50 µM) with increasing amounts of DNA from 10 µM to 100 µM. Each addition was left 10 min at 25 °C before was scanned from 230 nm to 600 nm.

Viscosity measurement

Viscosity measurements were performed using a Cannon Manning Semi-micro viscometer flooded in a thermostatic water bath at 37 °C. Flow times were manually measured with a digital stopwatch. From the observed flow times of the DNA-containing solutions (*t*), the viscosity values were calculated from the observed flow time of DNA-containing solutions (*t*) corrected for that of solvent mixture used (t_0), $\eta = t - t_0$. Viscosity data were given as $(\eta / \eta_0)^{1/3}$ versus [complex]/[DNA], where η and η_0 are the viscosity of the complex in the presence of DNA and the viscosity of DNA alone, respectively [24].

Synthesis of ligands

The ligands were prepared by the following general procedure in which a solution of corresponding aldehyde (4.483 mmol) of 4-methylbenzaldehyde (0.547 g), **1A**, or 4-methoxybenzaldehyde (0.61 g), **1B**, in ethanol (20 mL) was added to an ethanolic solution (20 mL) of semicarbazide (0.336 g). The mixture was refluxed with stirring for 2 h. The product was filtered, washed with ethanol, and air-dried. The ligands of **2A** and **2B** were prepared by the same procedure but in 2:1 molar ratio, in which a solution of corresponding aldehyde (8.966 mmol) of 4-methylbenzaldehyde (1.094 g) or 4-methoxybenzaldehyde (1.02 g), respectively.

(1A) M.p: 210-212 °C; Anal. Calc. for $C_9H_{11}N_3O$: C, 61.00; H, 6.26; N, 23.71, Found: C, 60.69; H, 6.38; N, 22.75; IR(KBr) ($\nu_{max/cm}^{-1}$): 3302 (s, C-N-H), 3147 (s, N-N), 1600 (s, C=N), 1550 (s, C=O); ^{1}H NMR (DMSO-d_6, ppm): 2.33 (s, CH_3), 6.48 (b, NH_2), 7.20, 7.62 (d, d, H-aromatic), 7.83 (s, CH=N), 10.18 (s, NH); ^{13}C NMR (DMSO-d_6,ppm): 20.98 (CH_3), 126.35 - 139.18 (C-aromatic), 140.84 (C=N), 156.29 (C=O).

(1B) M.p: 227-229 °C; Anal. Calc. for $C_9H_{11}N_3O_2$: C, 55.01; H, 5.74; N, 21.75, Found: C, 55.13; H, 5.82; N, 20.54; IR(KBr) ($\nu_{max/cm}^{-1}$): 3301 (s, C-N-H), 3146 (s, N-N), 1601 (s, C=N), 1557 (s, C=O); ^{1}H NMR (DMSO-d_6, ppm): 3.73 (s, CH_3), 6.48 (b, NH_2), 6.502, 7.66 (d, d, H-aromatic), 7.82 (s, CH=N), 10.19 (s, NH); ^{13}C NMR (DMSO-d_6,ppm): 55.06 (CH_3), 114.42 – 139.98 (C-aromatic), 157.01 (C=N), 161.96 (C=O).

(2A) M.p:222-224 °C; Anal. Calc. for $C_{17}H_{17}N_3O$: C, 73.09; H, 6.13; N, 15.04, Found: C, 72.84; H, 5.84; N, 13.99; IR(KBr) ($\nu_{max/cm}^{-1}$): 3393 (s, NH), 3261 (s, N-N), 1600 (s, C=N), 1553 (s, C=O); ^{1}H NMR (DMSO-d_6, ppm): 2.32, 2.43 (s, CH_3), 6.78, 6.99, 7.05, 7.38 (d, d, d, d, H-aromatic), 7.89 (s, CH=N), 9.48 (s, NH); ^{13}C NMR (DMSO-d_6,ppm): 14.43, 20.18 (CH_3), 110.09 – 135.05 (C-aromatic), 139.02, 149.69 (C=N), 170.03 (C=O).

(2B) M.p: 217-219 °C; Anal. Calc. for $C_{17}H_{17}N_3O_3$: C, 65.58; H, 5.50; N, 13.50, Found: C, 66.08; H, 5.82; N, 13.54; IR(KBr) ($\nu_{max/cm}^{-1}$): 3379 (s, NH), 3250 (s, N-N), 1610 (s, C=N), 1559 (s, C=O); ^{1}H NMR (DMSO-d_6, ppm): 3.74, 3.75 (s, CH_3), 6.955, 7.05, 7.57, 7.67 (d, d, d, d, H-aromatic), 7.775, 7.81 (s, CH=N), 10.18 (s, NH); ^{13}C NMR (DMSO-d_6,ppm): 55.08, 63.98 (CH_3), 114.46 – 132.99 (C-aromatic), 144.54, 155.02 (C=N), 179.03 (C=O).

Synthesis of complexes

The molybdenum complexes were prepared by the same general method: ethanolic solution in 1:2 molar ratio of $MoO_2(acac)_2$ (1.462 g, 4.483 mmol) and corresponding ligand of **1A** (1.586 g, 8.966 mmol), **2A** (2.5 g, 8.966 mmol), **1B** (1.73 g, 8.966 mmol) and **2B** (1.39g , 4.483 mmol) were mixed and refluxed for 2 h and then filtered. The filtrate was left to stand at room temperature, and the product was obtained after some days. The obtained complexes are assigned **C1A**, **C3A**, **C1B** and **C3B**, respectively. In respective, the complexes of C**2A** and C**2B** were prepared by the same procedure but in 1:1 molar ratio of corresponding ligands of **1A** (0.793 g, 4.483 mmol), **2A** (1.250g, 4.483 mmol) and, **1B** (0.865 g , 4.483 mmol) and **2B** (1.39g , 4.483 mmol).

(C1A) M.p:145-147 °C; Anal. Calc. for $C_{18}H_{20}N_6O_4Mo$: C, 45.01; H, 4.20; N, 17.50, Found: C, 44.79; H, 5.04; N, 16.82; IR(KBr) ($\nu_{max/cm^{-1}}$): 3407 (m, NH), 1590 (s, C=N), 1550 (m, C-O), 942, 902 (s, Mo=O); ^{1}H NMR (DMSO-d_6, ppm): 2.33 (s, CH_3), 6.506 (b, NH_2), 7.349, 7.705 (d, d, H-aromatic), 7.958 (s, CH=N); ^{13}C NMR (DMSO-d_6,ppm): 24.08 (CH_3), 143.46 – 154.91 (C-aromatic), 155.54 (C=N), 174.83 (C=O).

(C2A) M.p:205-208 °C; Anal. Calc. for $C_{26}H_{26}N_6O_4Mo$: C, 53.61; H, 4.50; N, 14.43, Found: C, 53.54; H, 4.55; N, 13.95; IR(KBr) ($\nu_{max/cm^{-1}}$): 3397 (m, NH), 1595 (s, C=N), 1550 (m, C-O), 938, 901 (s, Mo=O); ^{1}H NMR (DMSO-d_6, ppm): 2.01, 2.21, 2.33 (s, CH_3), 6.29 (b, NH_2), 6.59, 7.12, 7.20, 7.51, 7.57, 7.66 (d, d, d, d, d,d, H-aromatic), 7.92, 7.95, 8.01 (s, CH=N); ^{13}C NMR (DMSO-d_6,ppm): 24.08, 26.69, 32.03 (CH_3), 124.88 – 154.89 (C-aromatic), 165.98, 166.69 (C=N), 188.87, 191.07 (C=O).

(C3A) M.p:135-138 °C; Anal. Calc. for $C_{34}H_{32}N_6O_4Mo$: C, 59.65; H, 4.71; N, 12.28, Found: C, 60.16; H, 5.08; N, 13.13; IR(KBr) ($\nu_{max/cm^{-1}}$): 3303 (s, NH), 1587 (s, C=N), 1553 (s, C-O), 935, 901(s, Mo=O); ^{1}H NMR (DMSO-d_6, ppm): 2.09, 2.21 (s, CH_3), 7.68, 7.82, 7.99, 8.21 (d, d, d, d, H-aromatic), 8.73 (s, CH=N); ^{13}C NMR (DMSO-d_6,ppm): 25.08, 35.03 (CH_3), 121.88 – 136.79 (C-aromatic), 144.76, 153.69 (C=N), 190.86 (C=O).

(C1B) M.p: 128-130 °C; Anal. Calc. for $C_{18}H_{20}N_6O_6Mo$: C, 42.20; H, 3.93; N, 16.40, Found: C, 42.13; H, 3.54; N, 16.86; IR(KBr) ($\nu_{max/cm^{-1}}$): 3343 (s, NH), 1592 (s, C=N), 1564 (s, C-O), 933, 895 (s, Mo=O); ^{1}H NMR (DMSO-d_6, ppm): 3.71 (s, CH_3), 6.48 (b, NH_2), 6.95, 7.66 (d,d, H-aromatic), 7.82 (s, CH=N); ^{13}C NMR (DMSO-d_6,ppm): 55.97 (CH_3), 125.78 – 150.89 (C-aromatic), 167.98 (C=N), 172.08 (C=O).

(C2B) M.p: 153-157 °C; Anal. Calc. for $C_{26}H_{26}N_6O_7Mo$: C, 49.53; H, 4.16; N, 13.33, Found: C, 50.16; H, 3.99; N, 14.55; IR(KBr) ($\nu_{max/cm^{-1}}$): 3437 (m, NH), 1589 (s, C=N), 1563 (m, C-O), 938, 898 (s, Mo=O); ^{1}H NMR (DMSO-d_6, ppm): 3.45, 3.78, 3.97 (s, CH_3), 6.21 (b, NH_2), 6.59, 7.12, 7.20, 7.51, 7.57, 7.66 (d, d, d, d, d,d, H-aromatic), 7.92, 7.96, 8.01(s, CH=N); ^{13}C NMR (DMSO-d_6,ppm): 65.89, 69.87, 73.73 (CH_3), 124.88 – 154.89 (C-aromatic), 165.98, 166.69 (C=N), 188.87, 191.07 (C=O).

(C3B) M.p: 156-159 °C; Anal. Calc. for $C_{34}H_{32}N_6O_8Mo$: C, 54.55; H, 4.31; N, 11.23, Found: C, 55.08; H, 4.84; N, 11.55; IR(KBr) ($\nu_{max/cm^{-1}}$): 3447 (s, NH), 1589 (s, C=N), 1566 (s, C-O), 936, 901 (s, Mo=O); ^{1}H NMR (DMSO-d_6, ppm): 3.43, 3.57 (s, CH_3), 6.96, 7.05, 7.57, 7.67 (d, d, d, d, H-aromatic), 7.78, 7.81 (s, CH=N); ^{13}C NMR (DMSO-d_6, ppm): 65.98, 74.03 (CH_3), 125.08 – 150.97 (C-aromatic), 154.01, 165.98 (C=N), 188.95(C=O).

RESULTS AND DISCUSSION

Characterization

The ligands considered here were prepared in good yield by condensation of semicarazide with 4-methylbenzaldehyde and 4-methoxybenzaldehyde using ethanol as solvent. The elemental analysis (CHN) for the ligands and their complexes were in good agreement with those calculated for the suggested formula. The compounds were characterized by FTIR, ^{1}H NMR, ^{13}C NMR. All the compounds are air-stable and highly soluble in DMSO and DMF.

Infrared spectra

The important features of the IR spectra of the ligands are the appearance of a band at about 1600 cm^{-1} indicating the formation of the C=N group and the absence of free carbonyl and the primary amine bands. In general, the ligands exhibited very similar IR features. A ligand band at about 3379 cm^{-1} to 3393 cm^{-1} is attributed to υ (N–H) stretching, bands at about 3301 cm^{-1} corresponding to υ (C – N-H) group, a ligand band at about 1600 cm-1 is attributed to υ (C=N) group, bands at about 1612 cm^{-1} to 1622 cm^{-1} correspond to υ (C=N-N-C), the band at about 1550 cm^{-1} to 1559 cm^{-1} is assigned to the stretching frequency of the C=O bond.
The IR spectra of complexes show two sharp bands at about 938 cm^{-1} and 902 cm^{-1} assigned to antisymmetric and symmetric vibrations, respectively, of the Mo=O groups in *cis*–MoO_2^{+2} core (Rana et al., 2002). The IR bands of semicarbazone ligands have shifted to lower or higher frequencies upon chelation with MoO_2^{+2}. The stretching C–O band has been upward shifted to appeared in the region 1560-1568 cm^{-1}. The υ (C=N) underwent a change in frequency and intensity, to appeared at 1586-1590 cm^{-1}, indicating coordination of azomethine nitrogen [25].

^{1}H and ^{13}C NMR spectra

The ligands and their molybdenum complexes are exhibited ^{1}H and ^{13}C NMR spectra that consistent with their assigned structures (Figs. 1 and 2). In ^{1}H NMR spectra, the ligand **1A** shows the CH_3 protons as a singlet signal at 2.33 ppm, whereas it shifted to 3.73 ppm in the ligand **1B**. The broad signal appeared at 6.48 ppm that attributed to the protons of NH_2 group of **1A** and **1B** which is disappeared in spectra of **2A** and **2B**. The proton of azomethine group is emerged at 7.83 ppm, and the aromatic protons are appeared as doublet signals in the range from 6.78 ppm to 7.83 ppm.

In the ^{13}C NMR spectra, the ligand **1A** shows the carbon of CH_3 at 20.98 ppm, while the ligand **1B** shows it at 55.06 ppm. The aromatic carbons appeared in the range from 114.42 ppm to 139.98 ppm. The ligand of **1A** shows the carbons of C=N and C=O at 140.84 ppm and 156.29 ppm, **1B** at 157.01 ppm and 161.96 ppm, **2A** at 139.02, 149.69 and 170.03 ppm and, **2B** at 144.54, 155.02 and 179.03 ppm, respectively.

During the coordination with Mo (VI), the ligands in keto-form (-NH-C=O) changed to an enol form (-N=C-OH). The coordination induced proton chemical shifts are more pronounced for the CO-NH_2 and CH=N protons are shifted as a consequence of electron redistribution upon coordination with Mo (VI). On the other hand, the different chemical environment during coordination of two same ligands with Mo leads to double the NMR signals of protons.

In ^{1}H NMR spectra (Figs. 3 and 4), the ligand **C1A** shows the CH_3 protons as a singlet signal at 2.33 ppm, whereas it shifted to 3.71 ppm in the ligand **C1B**. The broad signals appeared at 6.506 ppm and 6.48 ppm are attributed to the protons of NH_2 group, the singlet signals arise at 7.958 ppm and 7.82 ppm are back to the proton of CH=N, the aromatic protons emerged as doublet signals at 7.349 ppm and 7.705 ppm and, 6.95 ppm and 7.66 ppm of **C1A** and **C1B**, respectively. The complexes of **C2A** and **C2B** show three of singlet signals at 2.01 ppm, 2.21 ppm and 2.33 ppm and, at 3.45 ppm, 3.78 ppm and 3.97 ppm are attributed to CH_3 protons, six of doublet signals at 6.59, 7.12, 7.20, 7.51, 7.57 and 7.66 ppm are attributed to aromatic protons and, three singlet signals at 7.92, 7.95 and 8.01 ppm, respectively. In contrast, The complexes of **C3A** and **C3B** show two of singlet signals at 2.09 ppm and 2.21 ppm and, at 3.43 ppm and 3.57 ppm are attributed to CH_3 protons, four of doublet signals at 7.68, 7.82, 7.99 and 8.21 ppm and, at 6.96, 7.05, 7.57 and 7.67 ppm are attributed to aromatic protons, respectively.

In ^{13}C NMR spectra (Figs. 3 and 4), the complex **C1A** shows the carbon of CH_3 at 24.08 ppm, while the complex **C1B** shows it at 55.97 ppm. The aromatic carbons appeared in the range from 125.78 ppm to 154.91 ppm. The ligand of **C1A** shows the carbons of C=N and C=O at 155.54 ppm and 174.54 ppm, **C1B** at 167.98 and 172.08 ppm, respectively. The complex **C2A** reveals three carbon signals for CH_3 group at 24.08, 26.69 and 32.03 ppm, while **C2B** reveals them at 65.89, 69.87 and 73.73 ppm and, the carbons of C=N emerged at 188.87 ppm and C=O emerged at 191.07 ppm. In contrast, The complex **C3A** reveals two carbon signals for CH_3 group at 25.08 ppm and 35.03 ppm, while **C3B** reveals them 65.98 ppm and 74.03 ppm, and double carbons signals emerged at 144.76 and 153.69 ppm in **C3A** and, at 154.01 ppm and 165.98 ppm in **C3B** are attributed to C=N group.

Binding with DNA

Absorption spectroscopic studies

Absorption spectroscopy is one of the most useful methods for DNA binding studies [26]. These studies show that the compounds can bind to DNA either through covalent bonding, such as in complexes that contain ligands which can be substituted with the nitrogen base of DNA, or by noncovalent interactions, such as intercalation and electrostatic or groove binding [27].

The samples were scanned from 200 nm to 600 nm and observed two intense absorption bands at high energy region attributed to π -π* transition at 230 and 285 nm. To determine the possible interactions with DNA, 10 µM of ligands or complexes were titrated with DNA in Tris-Buffer pH 7.2 at room temperature. Upon the addition a solution of DNA to the solutions of the ligands or their complexes, the intensity of the π -π* absorption band increases. This a spectral behavior indicates that the ligands and complexes are introduce a groove binding to the DNA at all concentrations (10 µM -120 µM) of DNA which may interact with back bone

of DNA polymer. Unlike, the ligand **1A** behaves an intercalator to DNA as long as the absorption intensity decreases with increases the DNA concentration, which may return to the planarity of **1A**. The planarity of compounds is an important factor in the intercalative binding with DNA. A good intercalator is that has a good planarity, which depends on the conformational structures as well as the geometrical configurations.

The binding strength of the ligands and their complexes was evaluated by calculating the intrinsic binding constant K_b. The absorption band at 285 nm was chosen to follow the changes in absorbance with increasing concentration of DNA using the following equation.

$$[DNA]/(\varepsilon_a - \varepsilon_f) = [DNA]/(\varepsilon_b - \varepsilon_f) + 1/(K_b\,(\varepsilon_b - \varepsilon_f)$$

wherein ε_a, ε_f, and ε_b are the apparent, free and bound molar extinction coefficients, respectively. K_b is the equilibrium binding constant (in M^{-1}) of compound binding to DNA. The binding constant is obtained by plotting $[DNA]/(\varepsilon_a - \varepsilon_f)$ vs [DNA]. The plots are incorporated in electronic absorption spectra of the ligand and complexes shown in Figs. 5 and 6. The obtained values of K_b are scheduled in table 1.

Table 1: Binding constants (M^{-1}) for ligands and their complexes

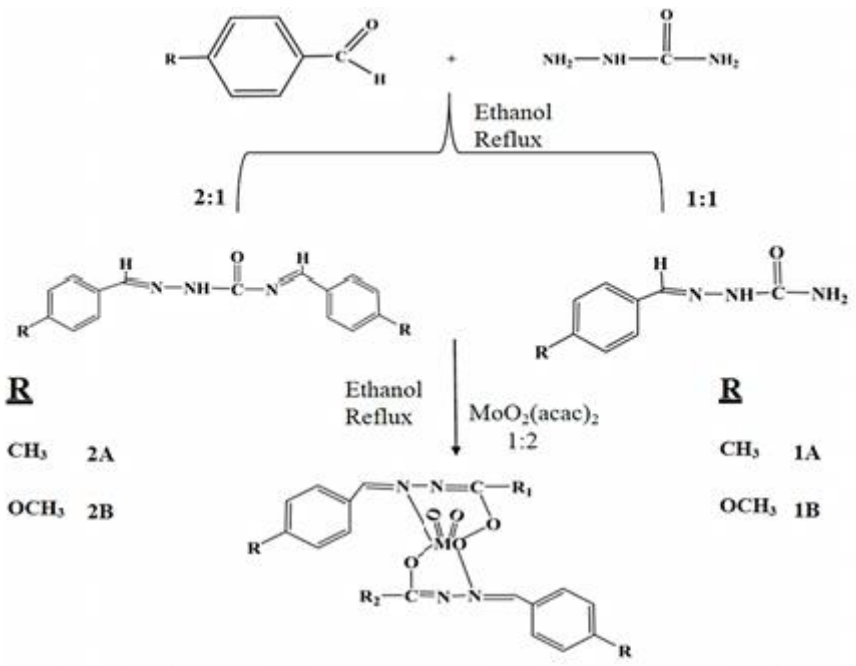
Compound	K_b (M^{-1})
1A	7.686×10^7
2A	3.684×10^7
1B	6.877×10^7
2B	3.313×10^7
C1A	3.807×10^8
C2A	1.944×10^8
C3A	4.724×10^8
C1B	6.004×10^8
C2B	2.961×10^8
C3B	3.638×10^8

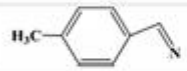
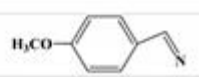
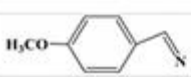
The obtained binding constants K_b show that the binding strength of the complexes is higher than that for the ligands, which reflect the affinity between the compounds and DNA. The ligand **1A** shows a significant binding strength compared to other ligands due to the intercalation binding mode with DNA that needs a sufficient strength extent to slide between the nitrogenous bases of DNA. The A set complexes of **C1A** and **C2A** are reveal less binding strength than B set complexes of **C1B** and **C2B**, while **C3A** shows more binding strength than **C3B**. These observations are indicate that the substituents of CH_3 and OCH_3 that located on 4-site of phenyl group have leading role with affinity between the compound and DNA.

Viscometric studies

Viscosity measurement is a main method for confer support to the non-covalent binding modes of compounds with DNA, and provides a simple common means of differentiating DNA binding mode. The groove binding does not cause major conformational changes in DNA, does not affect DNA helix length, and does not lead to increases the viscosity of DNA solutions. The changes in viscosity of the ligands and their complexes are shown in Fig. 7. Upon increasing the amount of the compound, the relative viscosity of DNA an irregularly and unapparent changed, this behavior displays that all the ligands and complexes, except that for **1A**, are bound with DNA in same manner, that of the groove binding mode but with different binding propensity. These results are consistent with the spectroscopic titration results [28].

Unlike the other compounds, the spectral results showed an intercalation binding mode between the ligand **1A** and DNA. Upon intercalation binding, the intercalator compound slides between nitrogenous bases of DNA causing conformational changes in DNA, lengthen the DNA helix, bent or tangled in the DNA helix and subsequently, increase the viscosity of DNA solutions, which is consistent with the spectral results.



R	R_1	R_2	compounds
CH_3	NH_2	NH_2	C1A
CH_3	NH_2		C2A
CH_3			C3A
OCH_3	NH_2	NH_2	C1B
OCH_3	NH_2		C2B
OCH_3			C3B

Scheme 1. Synthetic route and structures of the ligands and complexes

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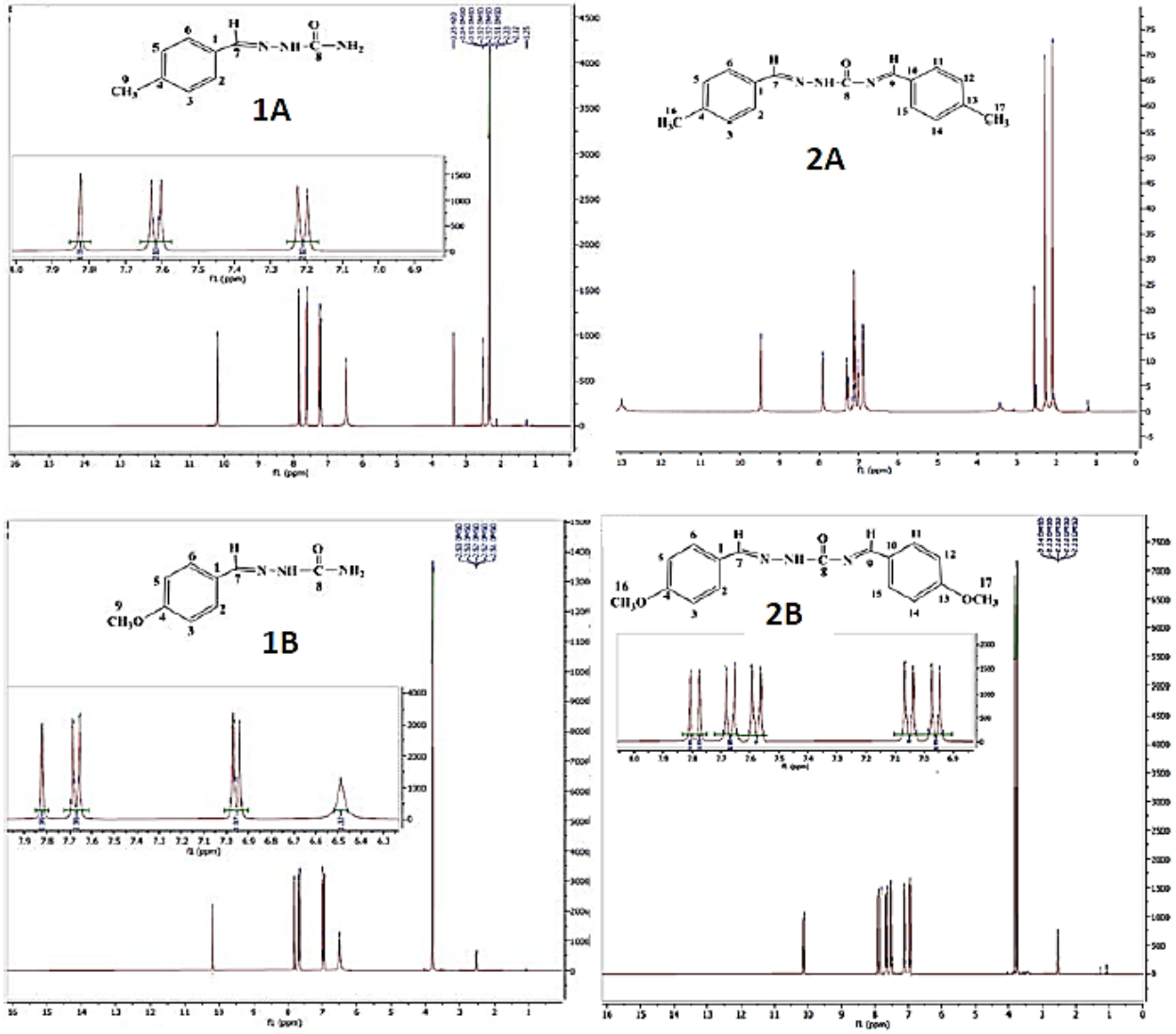

Fig. 1. ^{1}HNMR spectra of ligands

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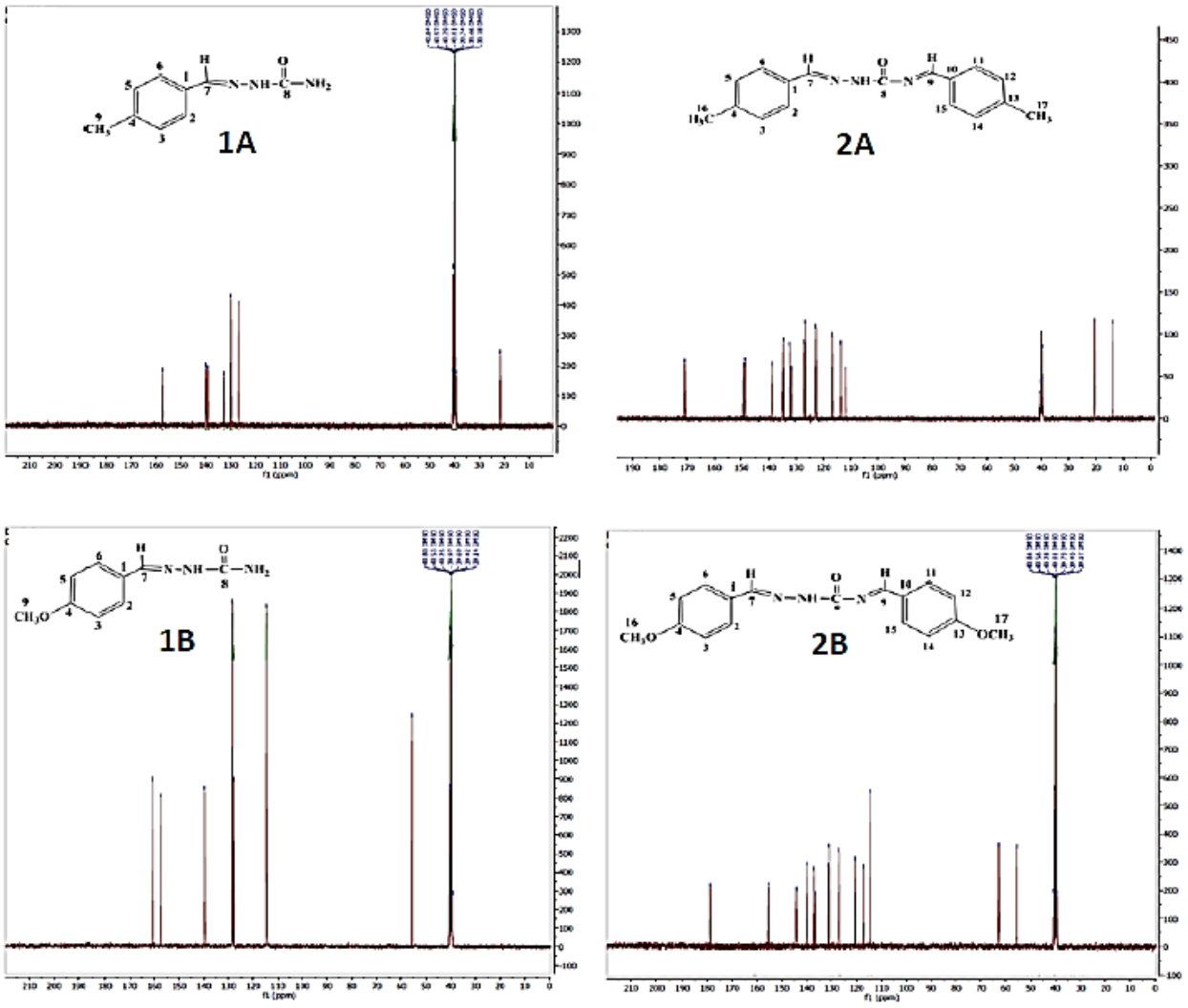

Fig. 2. ^{13}CNMR spectra of ligands

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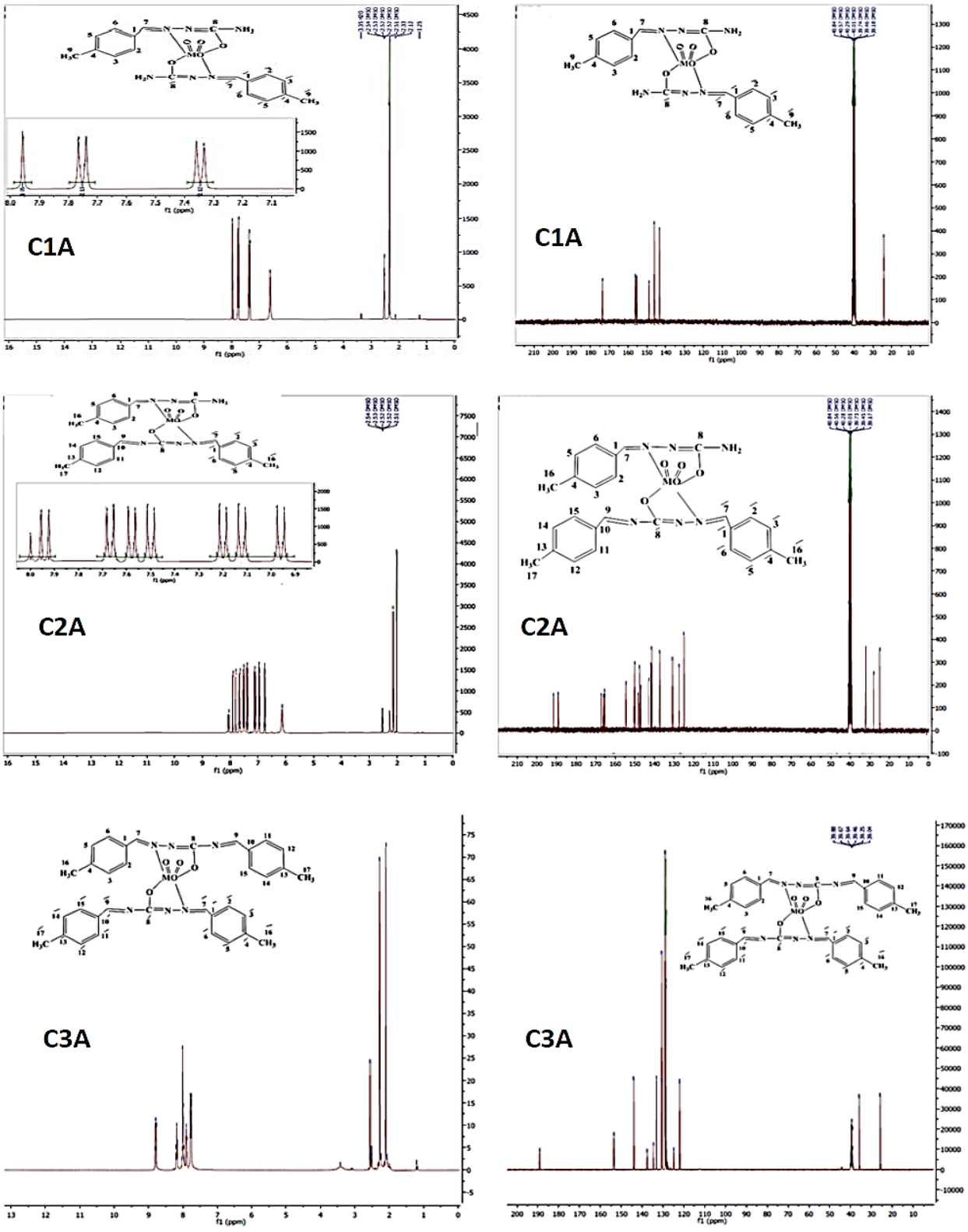

Fig. 3. NMR spectra of A-set complexes: left; ^{1}HNMR spectra, right, ^{13}CNMR spectra

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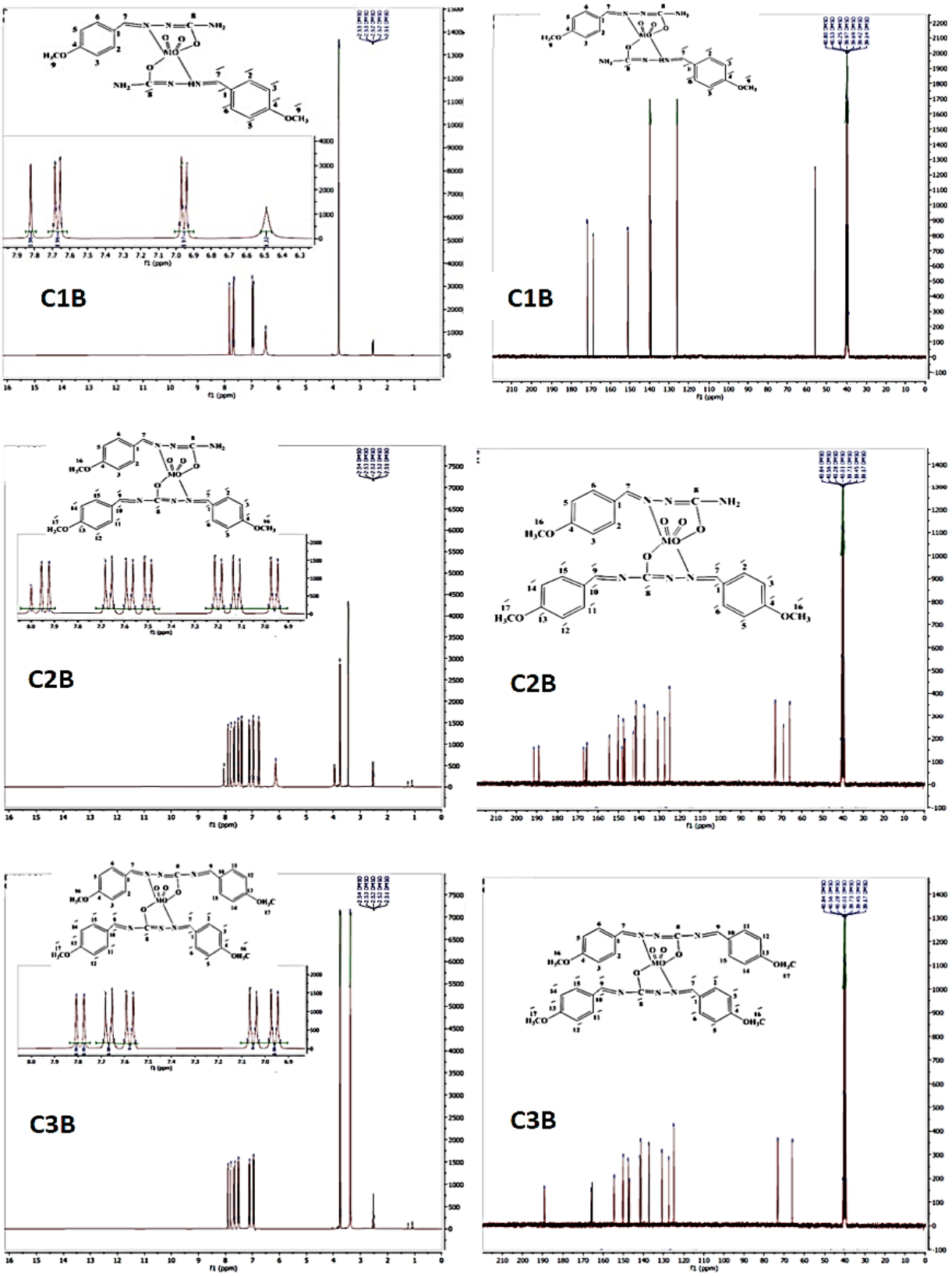

Fig. 4. NMR spectra of B-set complexes: left; ^{1}HNMR spectra, right, ^{13}CNMR spectra

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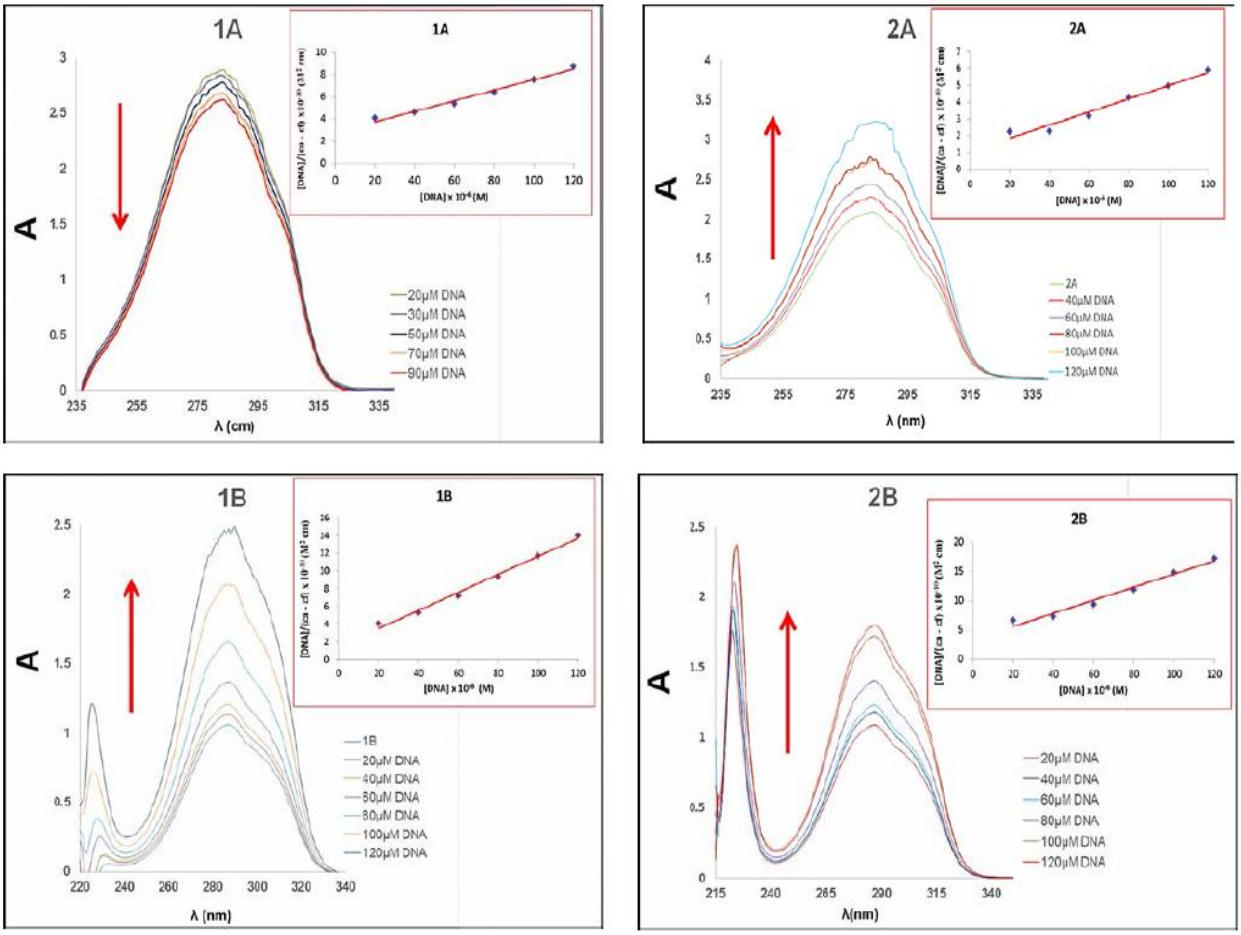

Fig. 5. Electronic spectra changes of ligands upon addition of DNA in tris HCl buffer solution; the inset is the plot of [DNA]/|(εa − εf) vs. [DNA]. The arrows show the changes in absorbance upon increasing amounts of DNA.

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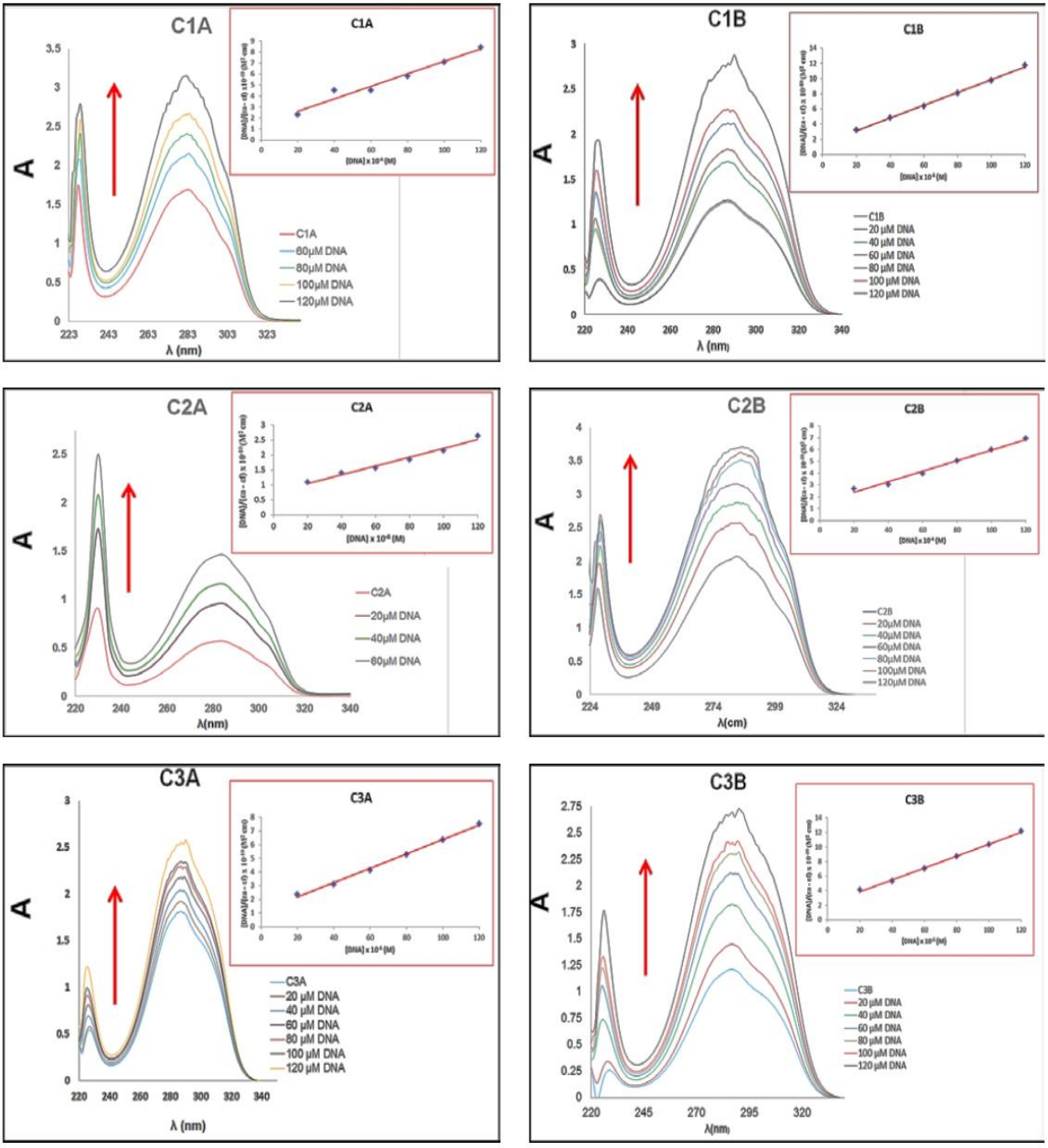

Fig. 6. Electronic spectra changes of complexes upon addition of DNA in tris HCl buffer solution; the inset is the plot of [DNA]/(εa − εf) vs. [DNA]. The arrows show the changes in absorbance upon increasing amounts of DNA.

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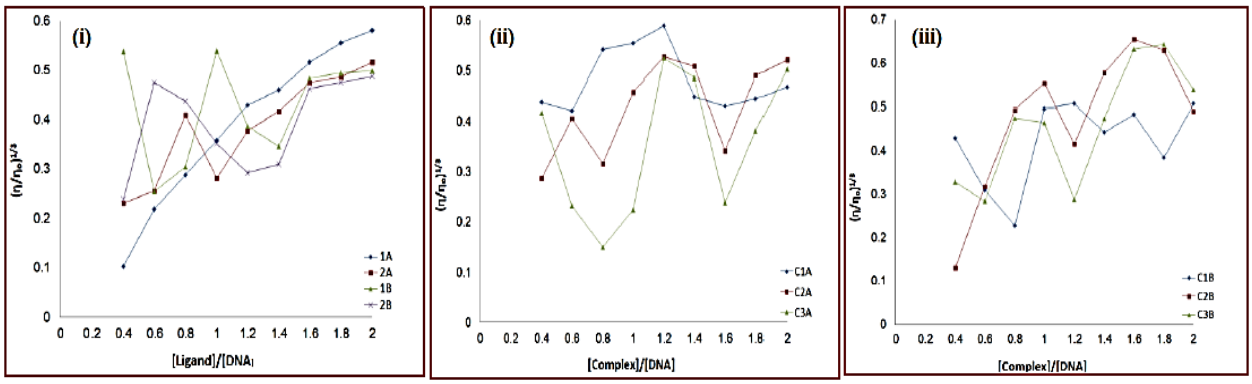

Fig. 7. Effect of increasing amounts; (i) ligands, (ii) A-set complexes and (iii) B-set complexes, on the relative viscosities of DNA in tris-HCl buffer solution

CONCLUSION

Six molybdenum (VI) complexes namely **C1A**, **C2A**, **C3A**, **C1B**, **C2B** and **C3B** derived from 4-methylbenzaldehyde or 4-methoxybenzaldehyde and semicarbazone namely **1A**, **2A**, **1B** and **2B** have been synthesized. The molecular structures of the compounds have been described by CHNS analysis, FTIR, ^{1}HNMR and ^{13}CNMR techniques. The interaction efficiency of the compounds with DNA was investigated by the spectroscopic and physical methods. The results revealed the groove binding mode between DNA and the compounds. The ligand **1A** revealed the intercalation binding with DNA. The binding constants were calculated and the results explained that the complexes have more binding strength than the ligands. Based on these findings, the complexes could be potentially useful in chemotherapy.

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