Synthesis, characterization and anticandidal activity of dioxomolybdenum(VI) complexes of the type \([\text{MoO}_2\{\text{ON}=\text{C}(\text{CH}_3)\text{Ar}\}_2]\) and \([\text{MoO}_2\{\text{OC}(\text{R})\text{CHC}(\text{R'})=\text{NC}_6\text{H}_5\}_2]\)

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1. Introduction

Molybdenum has been an important metal due to its capability of forming complexes with variety of ligands [1, 2, 3, 4], it is an essential constituent of recognized enzymes that catalyzes reduction of molecular nitrogen and nitrates in plants and oxidation (hydroxylation) of Xanthine and other Purines as well as aldehydes in animals [5]. Oxo- and dioxo-molybdenum complexes have been generously studied as catalysts for variety of organic transformations, commonly for sulfoxidation of sulfides [5], oxygen atom transfer (OAT) reactions [6, 7, 8, 9, 10, 11, 12]; antioxidant activities [13], and also as neutral esterification agents [14].

The variety of transition metal complexes with wide choice of oximes and Schiff’s bases ligand system and coordination environment have instigated us to undertake research in this area [15]. Complexes with Schiff base ligand systems have showed significant applications in many organic transformations as homogeneous and heterogeneous catalysts [16] such as in reduction of ketones to alcohols [17] and alkylation of allylic substrates [18, 19, 20]. Oxime metal chelates exhibit higher biological activity than corresponding free ligands [21]. Varied metallic complexes of oximes exhibited cytotoxicity in murine and human tissue cultured cell lines [22].

In continuation to our previous work [14, 23, 24, 25, 26] and to further study the chemistry of oxomolybdenum complexes incorporating oxygen, nitrogen and sulphur donor atoms; the synthesis of dioxomolybdenum(VI) complexes with internally functionalized oximes and Schiff’s bases derived from \(\beta\)-diketones is reported in present work.

2. Experimental

2.1. Materials and methods

2- acetyl thiophene, 2-acetyl furan, 2- acetyl pyridine, pentane 2,4 dione, 1-phenyl butane-1,3 dione, 1,3 diphenyl, propane-1,3 dione, acetylacetone and aniline (from Merck) were used as such. Hydroxylamine hydrochloride, sodium hydroxide and sodium acetate (from E. Merck) were used after drying at reduced pressure for 4–5 hours to ensure the complete removal of absorbed moisture. Precursor \([\text{MoO}_2(\text{acac})_2]\) was synthesized according to the literature method [27]. Oximes were synthesized by novel green methodology without using any organic solvent. Schiff bases of \(\beta\)-diketones were synthesized by literature method [28]. Molybdenum was estimated gravimetrically as oxinate. C and H were analyzed on a Perkin-Elmer C, H, N and S II series 2400 analyzer. Sulphur and nitrogen were estimated by standard methods. FT-IR spectra were recorded on a Perkin-Elmer spectrophotometer in the 4000-400 cm\(^{-1}\) range using KBr pellets. \(^1\)H-NMR spectra were recorded in CDC\(_3\) and d\(_6\)-DMSO using TMS as an internal reference on a JEOL.
2.2. Synthesis of oximes by green method

A solution of 2-acetyl thiophene (1.0g, 7.926 mmol) and hydroxylamine hydrochloride (0.55g, 7.926 mmol) in 10–12 ml water was stirred at 40–50 °C for half an hour. To this solution, sodium hydroxide pellets (0.32g, 7.926 mmol) were added portion wise and contents were stirred for another 2 hours at room temperature. The precipitate was collected by filtration, washed with distilled water and dried over P2O5 in vacuum.

All these products are yellow colored solids and are soluble in polar solvents like CH3OH, CH3CN, THF etc. except [MoO2(ON=C(CH3)2C6H4N)2] which remain sparingly soluble even in coordinating solvents like DMF and DMSO. Elemental analysis and m.p. of all the complexes have been summarized in Table 1.

3. Results and discussion

The interaction of [MoO2(acac)2] with internally functionalized oximes like HON=–(CH3)Ar (Ar=C6H5S, C6H5O or C6H5N) and Schiff bases derived from β-diketones like HOC(R)CHC(R')=NC6H5 (R=R'=CH3 or C6H5, R=CH3 and R'=C6H5) in 1:2 molar ratio in CH3OH has led to the formation of yellow dioxomolybdenum(VI) complexes of the types, [MoO2(ON=C(CH3)Ar)2] and [MoO2(OCH(R)CHC(R')=NC6H5)2].

All these products are yellow colored solids and are soluble in polar solvents like CH3OH, CH3CN, THF etc. except [MoO2(ON=C(CH3)2C6H4N)2] which remain sparingly soluble even in coordinating solvents like DMF and DMSO. Elemental analysis and m.p. of all the complexes have been summarized in Table 1.

3.1. IR Spectra

Some important IR spectral bands of complexes are summarized in Table 2. IR spectra of a representative complex [MoO2(ON=C(CH3)2C6H4N)2] and its parent ligand are provided as supplementary material (Figs. S1 and S2).

The absence of a signal in the spectra of the complexes, [MoO2(ON=C(CH3)Ar)2] and [MoO2(OCH(R)CHC(R')=NC6H5)2] due to

Table 2

| No. | Complex | S | cm⁻¹ | C–N (ring or C–=N) | C–C (β-diketone) | Mo–O |
|-----|---------|---|------|------------------|----------------|-----|
| 1   | [MoO2(ON=C(CH3)2C6H4N)2] | 1 | 1515 | 1930 (w) | 900 (s) |
| 2   | [MoO2(ON=C(CH3)2C6H4N)2] | 2 | 1500 | 1410 (w) | 905 (s) |
| 3   | [MoO2(ON=C(CH3)2C6H4N)2] | 3 | 1490 | 1450 (w) | 890 (s) |
| 4   | [MoO2(ON=C(CH3)2C6H4N)2] | 4 | 1620 (s) | 1400 (m) | 910 (s) |
| 5   | [MoO2(ON=C(CH3)2C6H4N)2] | 5 | 1610 (s) | 1380 (m) | 900 (s) |
| 6   | [MoO2(ON=C(CH3)2C6H4N)2] | 6 | 1605 (s) | 1370 (m) | 925 (s) |

The analytical results of both types of complexes are summarized in Table 1.

Table 1

Elemental Analysis and m.p. of [MoO2(ON=C(CH3)Ar)2] and [MoO2(OCH(R)CHC(R')=NC6H5)2].

| No. | Complex | C | H | N | S | Mo | M.p. (°C) |
|-----|---------|---|---|---|---|----|----------|
| 1   | [MoO2(ON=C(CH3)2C6H4N)2] | 34.52 (34.91) | 2.80 (2.88) | 6.63 (6.82) | 15.48 (15.73) | 23.33 (23.52) | 205 |
| 2   | [MoO2(ON=C(CH3)2C6H4N)2] | 37.98 (38.27) | 2.02 (3.19) | 7.18 (7.43) | - | 25.91 (25.48) | 200 |
| 3   | [MoO2(ON=C(CH3)2C6H4N)2] | 42.84 (42.23) | 3.61 (3.49) | 14.13 (14.04) | - | 24.05 (24.09) | 210 |
| 4   | [MoO2(ON=C(CH3)2C6H4N)2] | 55.03 (55.48) | 4.83 (4.91) | 5.82 (5.88) | - | 20.31 (20.24) | 173 |
| 5   | [MoO2(ON=C(CH3)2C6H4N)2] | 63.74 (64.04) | 4.63 (4.68) | 2.15 (2.28) | - | 16.14 (15.98) | 175 |
| 6   | [MoO2(ON=C(CH3)2C6H4N)2] | 69.14 (69.58) | 4.17 (4.35) | 3.47 (3.88) | - | 13.01 (13.18) | 180 |
ν (OH) in the 3600–3200 cm⁻¹ region suggests that ligands are bonded to molybdenum through the oxygen atom via deprotonation [28] (for IR details of ligands, refer Table S1 in supplementary data). This is further supported by two strong bands in the region 890-935 cm⁻¹ assigned to cis (Mo=O) symmetric and antisymmetric stretching vibrations [27, 29].

A weak band is observed in the free oximes in the range 1690–1640 cm⁻¹, characteristic of the azomethine (C=N) group has shifted to lower frequencies (1515-1490 cm⁻¹) in the spectra of the complexes of the type [MoO₂(ON=CH(R)Ar₂)]. Additionally, ν (C = X) (X = S, O or N) of aromatic ring in complexes were observed in the range 1450–1390 cm⁻¹ in IR spectrum. These values are lower than that observed for related free oximes in range 1490–1405 cm⁻¹ [30,31]; suggesting the bidentate behavior of the ligands.

The bands of ν (C=N) in the spectra of the complexes [MoO₂(OC(R)CHC(R')=NC₆H₅)] were observed in the region 1620-1605 cm⁻¹ indicating the formation of a coordinate bond through nitrogen to molybdenum atom [32]. These values are lower than that of free Schiff bases in region 1630-1620 cm⁻¹ characteristic of the azomethine (C=N) group [33]. Bidentate behavior of Schiff bases is further supported by bands of ν (C=O) symmetric and antisymmetric stretching vibrations [27, 29]. These values are lower than that of free Schiff bases in the 1515-1490 cm⁻¹ range. Bands of ν (C=O) in the 1760-1660 cm⁻¹ range, characteristic of the azomethine (C=O) group, are absent in the spectra of the above complexes [34].

The important electron absorption bands in the spectra of all these derivatives are compiled in Table 3. A comparison of peak positions in these complexes reveals their high dipolar character. Shifting of aromatic protons of the oxime moiety as well as of phenyl protons of the Schiff base to lower ppm value indicate bidentate behaviour of these ligands towards molybdenum(VI) moiety.

3.3. Electronic Absorption Spectra

The important electron absorption bands in the spectra of all these derivatives are compiled in Table 3. Dioxomolybdenum(VI) complexes of oxime derivatives [MoO₂(ON=CH(R)CHC(R')=NC₆H₅)] exhibit bands in 273–300 nm range which may be attributed to intraligand transitions [34]. Similarly, Schiff base derivatives, [MoO₂(OC(R)CHC(R')=NC₆H₅)] show such transitions at 307–317 nm [35].

Bands at 320–333 nm are characteristic of ligand to molybdenum(VI) charge transfer transitions in both types of complexes [27]. The absence of bands due to d-d transition in the range 650–420 nm supports the presence of molybdenum in +6 oxidation state.

3.3. ¹H NMR Spectra

The proton chemical shifts of these derivatives are summarized in Table 4. The OH signals present in the spectra of the free oximes and Schiff bases are found to be absent in the spectra of the above complexes showing deprotonation of the ligands, resulting in the formation of the desired products [28]. A comparison of peak positions in these complexes with those of their corresponding positions in the spectra of the free ligands [28, 30, 31, 32] reveals their high field shifting (ca 0.2–0.4 ppm), indicating bonding of the ligand moieties to the molybdenum atom.

| Table 3 | Some Relevant Electronic Absorption Spectral Data [λ max in nm] for [MoO₂(ON=CH(R)Ar₂)] and [MoO₂(OC(R)CHC(R')=NC₆H₅)] |
|---------|-------------------------------------------------------------------------------------------------|
| S. No.  | Complex                                                                                         | n→π⁺ | π→π⁺ | O=Mo⁶⁺ |
| 1       | [MoO₂(ON=CH(CH₃)CH₃)H₂]₂                                                                      | 365   | 210  | 318    |
| 2       | [MoO₂(ON=CH(CH₃)CH₂O)₂]                                                                       | 353   | 218  | 325    |
| 3       | [MoO₂(ON=CH(CH₃)CH₃N)₂]                                                                      | 375   | 213  | 315    |
| 4       | [MoO₂(OC(CH₃)CHC(CH₃)=NG₆H₅)₂]                                                                | 369   | 217  | 319    |
| 5       | [MoO₂(OC(CH₃)CHC(CH₃)=NG₆H₅)]                                                                | 370   | 215  | 315    |
| 6       | [MoO₂(OC(CH₃)CHC(CH₃)=NG₆H₅)]                                                                | 371   | 216  | 309    |

| Table 4 | ¹H-NMR Spectral Data (δ p.p.m.) of [MoO₂(ON=CH(CH₃)Ar₂)] and [MoO₂(OC(R)CHC(R')=NC₆H₅)] |
|---------|-------------------------------------------------------------------------------------------|
| S. No.  | Complex                                                                                         | δ H   |
| 1       | [MoO₂(ON=CH(CH₃)CH₃)H₂]₂                                                                      | 2.24  |
| 2       | [MoO₂(ON=CH(CH₃)CH₂O)₂]                                                                       | 2.15  |
| 3       | [MoO₂(ON=CH(CH₃)CH₃N)₂]                                                                      | 2.19  |
| 4       | [MoO₂(OC(CH₃)CHC(CH₃)=NG₆H₅)₂]                                                                | 2.17  |
| 5       | [MoO₂(OC(CH₃)CHC(CH₃)=NG₆H₅)]                                                                | 2.34  |
| 6       | [MoO₂(OC(CH₃)CHC(CH₃)=NG₆H₅)]                                                                | 3.81  |

| Table 5 | ¹³C (¹H) NMR Spectral Data (δ ppm) of [MoO₂(ON=CH(CH₃)Ar₂)] and [MoO₂(OC(R)CHC(R')=NC₆H₅)] |
|---------|---------------------------------------------------------------------------------------------|
| S. No.  | Complex                                                                                         | δ C   |
| 1       | [MoO₂(ON=CH(CH₃)CH₃)H₂]₂                                                                      | 11.9  |
| 2       | [MoO₂(ON=CH(CH₃)CH₂O)₂]                                                                       | 10.8  |
| 3       | [MoO₂(ON=CH(CH₃)CH₃N)₂]                                                                      | 20.4  |
| 4       | [MoO₂(OC(CH₃)CHC(CH₃)=NG₆H₅)₂]                                                                | 19.3  |
| 5       | [MoO₂(OC(CH₃)CHC(CH₃)=NG₆H₅)]                                                                | 92.6  |

Shifting of aromatic protons of the oxime moiety as well as of phenyl protons of the Schiff base to lower ppm value indicate bidentate behaviour of these ligands towards molybdenum(VI) moiety.

3.4. ¹³C (¹H) NMR Spectra

The ¹³C (¹H) NMR spectra of these complexes exhibit characteristic peaks for ligand carbon atoms. The data are summarized in Table 5. Down field shifting of C=N, C-2 and C-5 ary1 carbon signals of the oxime group as well as C=N and phenyl1 carbon signals of the Schiff base in ¹³C (¹H) NMR Spectra of these complexes as compared to the free ligands [30, 31] suggest bidentate behaviour of the ligands.

3.5. FAB Mass Spectra

Some of the most important mass spectral ion peaks of a typical oxime as well as a Schiff base derivative of dioxomolybdenum(VI), [MoO₂(ON=CH(CH₃)CH₃H₂N)₂] and [MoO₂(OC(CH₃)CHC(CH₃)=NG₆H₅)], with their tentative assignments are compiled in Tables 6 and 7. FAB mass spectrum of the [MoO₂(ON=CH(CH₃)CH₃H₂N)₂] exhibits the highest ion peak at m/z = 447, suggesting monomeric behavior of the complex with association of (CH₃)NO⁻ moiety.

Similarly the complex [MoO₂(OC(CH₃)CHC(CH₃)=NG₆H₅)] shows the highest ion peak at m/z = 899, indicating the presence of monomeric unit of the complex associated with (CH₃CO₂H₈)₂ moiety.

3.6. Anticandidal Activity

The in vitro evaluation of anticandidal activity for [MoO₂(ON=CH(CH₃)CH₃H₂N)₂] was carried out against Candida albicans in Dr. B. Lal Clinical Laboratory Pvt. Ltd. - Centre for Innovation, Research and Development (CIRD), Jaipur using Kirby-Bauer well diffusion method [36]. Compound was dissolved in DMSO at concentrations C1 = 10
Table 6
FAB mass spectral data of [MoO₂(NO-C(CH₃)C₆H₄N)]₂.

| m/e | Assignment |
|-----|------------|
| 447 | [MoO₂(NO-C(CH₃)C₆H₄N)C₂H₅NOH]⁻ |
| 440 | [MoO₂(NO-C(CH₃)C₆H₄N)]₂ |
| 371 | [MoO₂(NO-C(CH₃)C₆H₄N)C₂H₅CN] |
| 339 | [MoO₂(C₆H₆)-C₂H₅CN] |
| 289 | [MoO₂(C₆H₅N)C₂H₅CN] |
| 261 | [MoO₂(C₆H₅N)C₂H₅CN] |
| 232 | [MoO₂(C₆H₅N)C₂H₅CN] |
| 206 | [MoO₂(C₆H₅N)C₂H₅CN] |
| 192 | [MoO₂(C₆H₅N)C₂H₅CN] |
| 149 | [MoO₂(C₆H₅N)C₂H₅CN] |
| 137 | [MoO₂(C₆H₅N)C₂H₅CN] |

Table 7
FAB mass spectral data of [MoO₂(C₆H₅N)CHC(C₆H₅)])₂.

| m/e | Assignment |
|-----|------------|
| 899 | [MoO₂(C₆H₅N)CHC(C₆H₅)])₂C₂H₅CN |
| 752 | [MoO₂(C₆H₅N)CHC(C₆H₅)])₂C₂H₅CN |
| 712 | [MoO₂(C₆H₅N)CHC(C₆H₅)])₂C₂H₅CN |
| 688 | [MoO₂(C₆H₅N)CHC(C₆H₅)])₂C₂H₅CN |
| 609 | [MoO₂(C₆H₅N)CHC(C₆H₅)])₂C₂H₅CN |
| 560 | [MoO₂(C₆H₅N)CHC(C₆H₅)])₂C₂H₅CN |
| 473 | [MoO₂(C₆H₅N)CHC(C₆H₅)])₂C₂H₅CN |
| 396 | [MoO₂(C₆H₅N)CHC(C₆H₅)])₂C₂H₅CN |
| 351 | [MoO₂(C₆H₅N)CHC(C₆H₅)])₂C₂H₅CN |
| 225 | [MoO₂(C₆H₅N)CHC(C₆H₅)])₂C₂H₅CN |
| 154 | [MoO₂(C₆H₅N)CHC(C₆H₅)])₂C₂H₅CN |
| 136 | [MoO₂(C₆H₅N)CHC(C₆H₅)])₂C₂H₅CN |

Table 8
Anticandidal activity of [MoO₂(NO-C(Ch₃)C₆H₄N)]₂.

| Compound | Zone of Inhibition (mm) |
|----------|------------------------|
| NC - DMSO | Nzi |
| [MoO₂(NO-C(Ch₃)C₆H₄N)]₂ at C1 | Nzi |
| [MoO₂(NO-C(Ch₃)C₆H₄N)]₂ at C2 | 14 |
| PC - Amphotericin B (50μg) | 2 |

NZI - No zone of inhibition.

Fig. 1. Anticandidal activity of [MoO₂(NO-C(Ch₃)C₆H₄N)]₂.

mg/mL⁻¹ and C2 = 100 mg/mL⁻¹ concentrations; Amphotericin B was used as PC- positive control at 50 μg/ml concentration and DMSO was used as NC- negative control. Results of anticandidal activity are listed in

4. Conclusion

In absence of crystal structure which may be due to the amorphous nature of the synthesized novel molecules, we cannot put forward the exact structures of the respective compounds; but in view of the above elemental and spectral studies, we may propose that all the complexes synthesized can be represented as [MoO₂L₂] (where L = corresponding ligand; oxime/schiff base). Anticandidal activity has been carried out on [MoO₂(NO-C(Ch₃)C₆H₄N)]₂ which clearly reveals that the complex is biologically active.

Declarations

Author contribution statement

Deepankar Sharma: Performed the experiments; Wrote the paper.
Purnima Nag: Conceived and designed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

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Additional information

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