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FULL PAPER

Synthesis and characterization of binary and ternary oxovanadium complexes of *N*,*N*′-(2-pyridyl)thiourea and curcumin: Catalytic oxidation potential, antibacterial, antimicrobial, antioxidant and DNA interaction studies

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Two binary and two ternary mono-oxovanadium (IV) complexes of acetylacetonate, curcumin and *N*,*N*′-bis(2-pyridyl)thiourea were synthesized. They were characterized using elemental analysis, infrared and UV–visible spectroscopies and magnetic and conductivity measurements. The formation constants K_f were determined from spectrophotometric measurements. The catalytic potential of the VO complexes was investigated for the oxidation of 1-octene by aqueous H_2O_2 in acetonitrile. They display high catalytic potential for the conversion of 1-octene with low chemoselectivity to the epoxy product. The VO complexes exhibit good antibacterial and antimicrobial activities. The antioxidant activity of the VO complexes and their ligands was investigated. The VO complexes show high DNA affinity and DNA cleavage ability.

KEYWORDS

1-octene, antibacterial, antimicrobial, antioxidant, catalytic oxidation, curcumin, DNA, oxovanadium (IV), pyridylthiourea

1 | INTRODUCTION

Coordination chemistry of vanadium is experiencing strong development with highlights in important fields of biological, medicinal, material and organic syntheses.[1] Particularly, catalytic (ep)oxidation is of interest in the field of organic syntheses. Indeed, vanadium displays various oxidation states, especially easily accessible high oxidation states (oxovanadium(IV), VO^{2+}) with a variety of coordination numbers and a high affinity for oxygen donation. This behaviour could help its application in redox and Lewis acid catalysed or promoted reactions.[2,3] Oxovanadium(IV) complexes are some of the most effective and efficient catalysts for the oxidation of hydrocarbons both homogeneously and heterogeneously.[4,5] Aqueous H_2O_2 is one of the most applicable oxidants in organic oxidation processes because it affords only water as a by-product and it is more accessible and less expensive compared to other oxidizing agents. Furthermore, it is more environmentally friendly. H_2O_2 is highly active for the oxidation of organic compounds with low chemo- and regioselectivity compared to other organic oxidants, e.g. *tert*-butyl hydroperoxide.[6]

Curcumin is one of the most important reagents for pharmaceutical applications.[7–9] It is much used as an arthritis treatment,[10] an anti-inflammatory agent[11] and an oral diabetes treatment.[12] Complexation of curcumin with transition metals has been widely studied, e.g. with boron, iron, copper,[13,14] chromium, nickel,[14] lanthanum[15] and rare earth metals.[16] The coordination behaviour of curcumin with oxovanadium(IV) ions has been investigated previously, acting as a bidentate ligand.[17,18] A comparison of the inhibition effect of oxovanadium dicurcumin complex and free curcumin for synoviocyte, smooth muscle cell and mouse lymphoma cell proliferation was reported by Thompson *et al.*[17] Oxovanadium(IV) curcuminoid complexes show high photoactivated cytotoxicity in visible light.[19] To the best of our knowledge, there is no literature reports concerning the coordination of oxovanadium(IV)

with *N*,*N*′-dipyridylthioura. There have been extensive studies[20–22] of the structures of *N*,*N*′-(substituted-2-pyridyl)thioureas and their intra−/intermolecular hydrogen bonding interactions. *N*,*N*′-bis(substituted-2-pyridyl) thioureas with Cu(I) and Zn(II) ions have been reported.[23]

Due to the high applicability of oxovanadium(IV)–curcumin complexes especially in medicinal fields and in continuation of previous work on the coordination behaviour of *N*,*N*′-(2-dipyridyl)thiourea with various transition metals, Pt(II), Pd(II), UO_2(II),[24] this paper presents the synthetic routes to four binary and ternary VO complexes derived from the coordination of acetylacetonate (ac), curcumin (cur) and *N*,*N*′-bis(2-pyridyl)thiourea (NS) with mono-oxovanadium(IV) ion. The catalytic potential of these VO complexes was investigated for the oxidation of 1-octene, as an example of an unsaturated hydrocarbon, with aqueous H_2O_2.

2 | RESULTS AND DISCUSSION

2.1 | Characterization of VO complexes

The synthesized VO complexes are soluble in dimethylsulfoxide (DMSO) and dimethylformamide, and poorly soluble in polar solvents, e.g. methanol and acetone. The pH of VO complex solutions (1×10^{-4} mol dm^{-3}) is almost stable in the neutral range from pH ~ 4.1 to 8.7. They are unstable in strong basic and acidic media where the color decays. All complexes decompose at high temperatures as reported in Table 1.

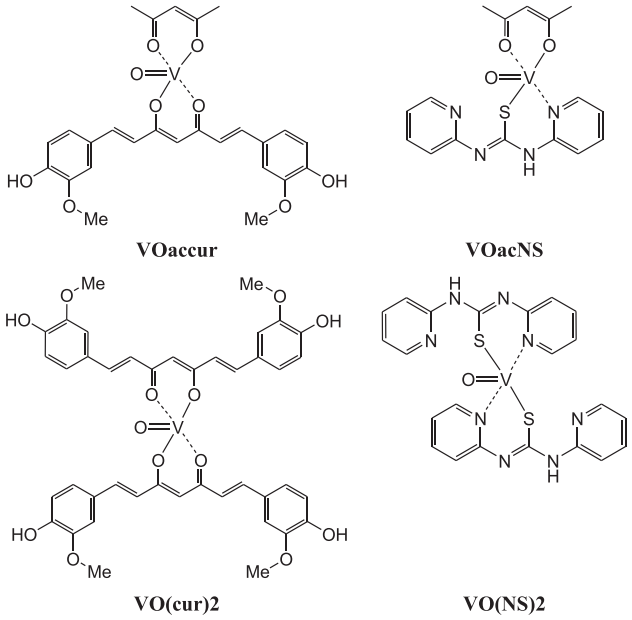
The characteristic data for the VO complexes are compared with those reported for the corresponding VO(cur)2[17] in order to confirm the coordination mode. The CHN microanalysis values of all complexes are in good agreement (±0.6%) with the expected structure (Table 1). VO complexes are assumed to be in a mole ratio of 1:2 (metal:ligand) forming chelated neutral bis-complexes as binary complexes, VO(NS)2 and VO(cur)2, and ternary complexes, VOaccur and VOacNS, as shown in Scheme 1.

The electronic absorption spectra of ligands cur and NS, and of their corresponding VO complexes were recorded in the wavelength range 200–700 nm and at 298 K (Figure 1). The wavelengths at maximum absorption (λ_{max}) and the molar absorptivity (ε) of the various bands of the VO complexes are given in Table 1. An intense band in the range from 245 to 287 nm is assigned to a $\pi \rightarrow \pi^*$ transition originating in the aromatic moiety. A band at 297 nm for VO(NS)2 may be attributed to $n \rightarrow \pi^*$ transition originating for the electrons localized on the chromophore C═N or C═S, due to an intramolecular charge transfer transition taking place in the coordinated ligand.[25] A band in the region 363–464 nm could be attributed to the charge transfer from ligand to metal (Table 1). The electronic spectra of VO complexes exhibit a

TABLE 1 Characteristic elemental analysis, melting point, appearance and electronic spectra of the VO complexes (1×10^{-4} mol dm^{-3} at 25 °C)

Complex	MW (g mol^{-1})	Microanalysis (%): found (calcd)			Appearance	M.p. (°C)	Electronic spectra (in DMSO)		
		C	H	N			λ_{max} (nm)[a]	ε_{max} (mol^{-1} cm^{-1})	Assignment
VOaccur	533.42	59.27 (58.54)	4.40 (4.91)	Nil (Nil)	Red	>300	628 v br 421 245	390 11120 14820	d → d LM-CT π → π*
VOacNS	395.33	47.93 (48.61)	4.08 (4.05)	13.85 (14.17)	Pale green	215	632 v br 363 296 287	310 2640 4260 4010	d → d LM-CT n → π* π → π*
VO(NS)2	801.68	50.70 (50.28)	4.02 (3.45)	21.89 (21.32)	Green	244	556 br 365 297 285	280 4170 5010 9750	d → d LM-CT n → π* π → π*
VO(cur)2	525.50	61.67 (62.26)	4.11 (4.18)	Nil (Nil)	Reddish brown	250	600 v br 464 270	280 8630 2200	d → d LM-CT π → π*

[a]v br = very broad band.



SCHEME 1 Tentative molecular structures of VO complexes

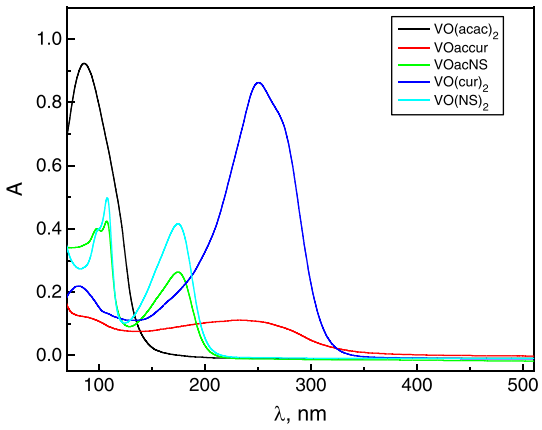


FIGURE 1 Molecular spectral scan of the VO complexes ([complex] = 1×10^{-4} mol dm^{-3} in DMSO at 25 °C)

band in the range 556–632 nm assignable to a $^2E_g \rightarrow {}^2T_g$ transition characteristic of structural geometry.[26]

Infrared (IR) spectral data for the synthesized complexes and their corresponding ligands[14,24] are listed in Table 2. On complexation, the appearance of a new band characteristic for the azomethine $\overline{\nu}_{(C=N)}$ at 1651 and 1652 cm^{-1} for VO(NS)2 and VOacNS, respectively, is significant for the proton tautomeric shift from nitrogen to sulfur, $\overline{\nu}_{(SH-C=N)}$, i.e. deprotonation of NS during complexation with VO^{2+} ion. Moreover, the observable shift of the $\overline{\nu}_{(C=Npy)}$ band from 1603 cm^{-1} to 1620 and 1612 cm^{-1} for VO(NS)2 and VOacNS, respectively, is very probably due to the involvement of the N-pyridine in the coordination. The formation of the metal–nitrogen bond stabilizes the electron pair on the nitrogen pyridine.[27]

For VOacNS, the presence of a strong band at 1651 cm^{-1} and a weak band at 1519 cm^{-1} is attributed to coordination of the actylacetonate group through C═O and C─O groups, respectively, to VO^{2+} ion (Table 2).

On the other hand, VO(cur)2 and VOaccur show an observed shift of the $\overline{\nu}_{(C=O)}$ at 1589 and 1652 cm^{-1}, respectively, compared to the corresponding band for curcumin or acetylacetonate (1628 cm^{-1}). The presence of a broad $\overline{\nu}_{(OH)}$ band at 3649 and 3425 cm^{-1} for VO(cur)2 and VOaccur, respectively, assigned to the hydroxyl group compared to that band in the free ligand at 3508 cm^{-1} due to the effect of coordination. The appearance of a new $\overline{\nu}_{(V=O)}$ band at 925–995 cm^{-1} corresponds to the V═O group in the complexes (Table 2).

The conductivity measurements carried out in DMSO produce very low values as recorded in Table 3. The results demonstrate that all binary and ternary VO complexes are non-electrolytic. Hence, for the general formula of the VO complexes, it is suggested that ac, cur and NS ligands act as monobasic bidentate ligands, as shown in Scheme 1.

TABLE 2 Structural significant IR spectral data ($\overline{\nu}$, cm^{-1}) of the VO complexes[a]

Group	VOaccur	VOacNS	VO(NS)2	VO(cur)2	NS ligand[24]	cur ligand[12]
O─H	3425(br, s)			3649 (br, s)		3508
C─O	1280 (br, s)			1211 (m)		
NH		3749 (br, w) 3394 (br m)	3749 (w) 3440 (br s)			
C─N		1319 (m)	1319 (w)			
$C-H_{ar}$	3085 (w)	3062 (m) 3024 (m)	3055 (w)	3029 (w)		
$C-H_{alph}$	2939 (w)	2869 (w)		2987 (w)		
C═O	1589 (m)	1651 (m)		1697 (m)		1628
C─O	1512 (s)	1519 (s)		1502 (m)		1427
$C=N_{(py)}$		1612 (s)	1620 (m)		1603	
$C=N_{(azomethine)}$		1652 (m)	1651 (m)			
C═C	1458 (m)	1542 (m)	1512 (s)	1512 (m)		1507
C─C	1380 (w)	1419 (m)	1434 (m)	1380 (m)		
V═O	925 (m)	987 (m)	955 (m)	995 (m)		
C═S					787	

[a]br = broad band, s = strong, m = moderate band, w = weak band, ar = aromatic ring, alph = aliphatic chain.

TABLE 3 Characteristic magnetic moments (μ) and molar conductivities (Λ_m) of VO complexes (concentration in electrolyte $=1 \times 10^{-4}$ mol dm^{-3}) in DMSO at 25 °C

Complex	μ (BM)	Λ_m (Ω^{-1}·cm^2·mol^{-1})
VOaccur	0.221	1.883
VOacNS	0.568	1.737
VO(NS)2	1.189	1.457
VO(cur)2	1.268	1.551

Magnetic susceptibility measurements (Table 3) of the binary and ternary VO complexes suggest that all complexes are of high spin and paramagnetic in a square pyramidal geometrical structure in the range 0.22 to 1.26 BM.[17] Those values indicate that there is no possibility for interaction between vanadium atoms. The coordination of the square pyramidal structure as a closed system impacts on their solubilities by decreasing in polar solvents (Scheme 1). Unfortunately, all attempts to characterize the complex structure by single-crystal X-ray analysis were unsuccessful, with synthesis affording powders.

2.2 | Determination of thermodynamic parameters of VO complexes

The stoichiometry of the binary and ternary VO complexes was determined by spectrophotometric continuous variation methods.[28,29] Their application to the investigated complexes confirm the 1:1 metal-to-ligand (NS or cur) molar ratios in the ternary complexes (VOacNS and VOaccur) as shown in Figure S1 (supporting information). For the binary complexes (VO(NS)2 and VO(cur)2), metal-to-ligand (NS or cur) molar ratios were 1:2, as shown in Figure S2 (supporting information). The formation constants K_f of the VO complexes were determined from spectrophotometric measurements according to the following equation derived from the continuous variation method[30]:

$$K_f = \frac{A/A_m}{[1-(A/A_m)]^2 C} \quad (1)$$

where A_m is the absorbance at the point of the most complete complex formation according to the continuous variation plot (Figures S1 and S2) and A is the absorbance of the complex at the arbitrarily chosen metal ion concentration C. The derived data collected in Table 4 indicate high stability of the prepared VO complexes. The values of K_f for the studied complexes reflect the decrease of substitution reaction of NS or cur with one ac ion in VOaccur and VOacNS or two ions in VO(cur)2 and VO(NS)2, and goes in the following series: VOaccur > VOacNS > VO(cur)2 > VO(NS)2.

From the determined equilibrium formation constants at various temperatures, we managed to determine the thermodynamic parameters of complex formation. According to the Gibbs–Helmholtz equation (equation (2)), $\Delta_f H$ and $\Delta_f S$ are determined from the slope and intercept, respectively, of a linear plot of ln K_f as a function of $1/T$ (Figure 2):

$$\frac{\Delta_f G}{T} = -R \ln K_f \quad (2)$$

TABLE 4 Stability constants and thermodynamic parameters of VO complexes ([VO complex] = 1×10^{-4} mol dm^{-3})

Complex	T (°C)	K_f ($\times 10^9$ l mol^{-1})	$\Delta_f G$ (kJ mol^{-1})	$\Delta_f H$ (kJ mol^{-1})	$\Delta_f S$ (J mol^{-1} K^{-1})
VOaccur	20	4.98	−54.39	2.55	13.60
	25	4.12	−54.84		
	30	3.63	−55.45		
	35	3.27	−56.10		
	40	2.79	−56.59		
VOacNS	20	4.67	−54.23	2.96	12.16
	25	3.97	−54.75		
	30	3.32	−55.04		
	35	2.82	−55.72		
	40	2.48	−56.29		
VO(NS)2	20	4.38	−54.08	3.45	10.39
	25	3.56	−54.49		
	30	2.91	−54.83		
	35	2.43	−55.34		
	40	2.07	−55.82		
VO(cur)2	20	4.48	−54.13	2.93	12.23
	25	3.90	−54.71		
	30	3.51	−55.37		
	35	2.76	−55.67		
	40	2.39	−56.19		

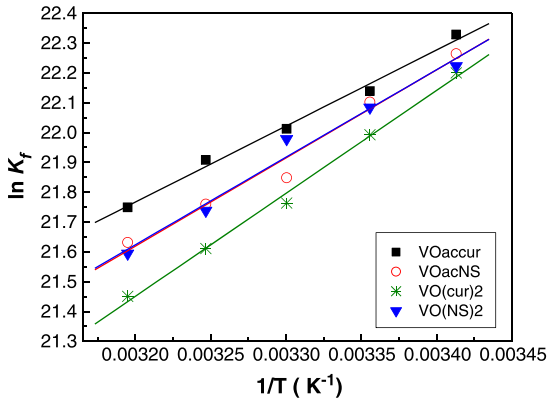


FIGURE 2 Determination of thermodynamic parameters of VO complex formation from ln K_f values

The derived parameters are given in Table 4. The negative values of $\Delta_f G$ reflect spontaneous complex formation under all the studied conditions. As $\Delta_f H$ is negative, the reaction is exothermic, and the formed metal–ligand bonds are fairly strong.[31]

2.3 | Catalytic potential

The collected oxidation reaction products of 1-octene using 30% aqueous H_2O_2 were analysed by GC-MS. Analysis was performed by injection of 1 µl of each sample in the GC injection port. The obtained (ep)oxidation products of

TABLE 5 Catalytic oxidation product percentages of 1-octene using aqueous 30% H_2O_2 catalysed by VO complexes[a]

VO complex	1-Octene	Octanal	7-Octen-2-one	Octane-1,2-epoxy	2-Octenal	1-Octanoic acid	1,2-Octanediol	Other products
VOaccur	18.42	10.15	1.58	1.17	2.06	4.52	15.93	64.58
VOacNS	2.92	6.09	1.74	0.78	1.53	1.46	14.49	73.9
VO(NS)2	0.52	4.88	1.52	1.27	1.6	4.05	17.22	68.93
VO(cur)2	5.02	5.29	2.67	1.56	2.65	0.23	16.31	70.68

[a]Oxidation of 1-octene (1.0 mmol) by aqueous H_2O_2 (3.00 mmol) catalysed by VO complexes (0.02 mmol) in 10 ml of acetonitrile for 16 h, at 50 °C.

1-octene using aqueous H_2O_2 are summarized in Table 5. It is well known that the chemoselective product, as main product, of the catalytic oxidation of 1-octene is octane-1,2-epoxy.[32] However, such selectivity depends upon the type of catalytic process.[33] Catalytic oxidation of 1-octene as a representative model of alkenes by aqueous H_2O_2 as external oxidant catalysed by VO complexes at 50 °C for 16 h affords various oxidation products with varying percentages (Table 5) of octanal, 7-octen-2-one, octane-1,2-epoxy, 2-octenal, 1-octanoic acid and 1,2-octanediol. However, the VO complexes show high catalytic potential; their chemoselectivity is low for the oxidation of 1-octene. Furthermore, the quantitative and qualitative reaction products depend upon the nature of the VO complex catalyst. The catalytic conversion activity of all VO complexes for 1-octene oxidation is quite high with very low chemoselectivity. VOacNS and VO(NS)2 have higher catalytic potential than VOaccur and VO(cur)2. It seems that the coordinated ligand ac, NS or cur has a remarkable effect on the catalytic potential of the VO complexes sterically and electronically.[34] Electronically, the donor O-atom of the coordinated ligands (ac and cur) forms more stable and closed complexes with VO^{2+} ion than the N- and S-atoms of the coordinated ligand (NS), i.e. VO(NS)2 and VOacNS, as observed for vanadyl complexes by Rayati et al.[35] The steric effect can be also observed in the catalytic potential of VO complexes in the oxidation process of 1-octene.[34,36] The steric effect can be observed on the catalytic potential of VOaccur and VO(cur)2 which is low compared to that of VOacNS and VO(NS)2. From the molecular structure of VOaccur and VO(cur)2, as seen in Scheme 1, VO(cur)2 is less stable sterically compared to VOaccur which may be the reason for the high catalytic potential of VOaccur (Table 5). The electronic and steric effects[3,37] on the catalytic potential of the VO complexes could be a result of electron or oxygen transfer to the central metal ion in the catalytic processes. Particularly, the more stable VO complexes are the less reactive as catalysts for the oxidation of 1-octene, as evident from Tables 4 and 5.

2.4 | Biological activities

2.4.1 | Antibacterial activities

The antimicrobial activities of cur and NS as ligands and the corresponding synthesized VO complexes VOaccur, VOacNS, VO(NS)2 and VO(cur)2 were examined against both Gram-negative and Gram-positive bacteria using only one concentration of them in DMSO. The control utilized was DMSO alone. The inhibition zones against the growth of the verified bacteria of the synthesized VO complexes are given in Table 6. It is clear that the VO(cur)2 complex exhibits the greatest antimicrobial activity as expressed by inhibition zone diameter towards *Escherichia coli* (18 mm), *Pseudomonas aeruginosa* (17 mm), *Staphylococcus aureus* (20 mm) and *Bacillus megaterium* (18 mm). Ampicillin as a medical antibiotic exhibits antimicrobial activity towards *E. coli* (21 mm), *P. aeruginosa* (20 mm), *S. aureus* (22 mm) and *B. megaterium* (20 mm). The cur ligand and VOaccur reveal good antimicrobial activity towards the examined microorganisms. However, NS, VOacNS and VO(NS)2 reveal the lowest antimicrobial activity. There is a clear correlation between the structure of the studied VO complexes and their microbial activity. Evidence shows that the formation of the electron donor groups increases the biological activities of cur, VOaccur and VO(cur)2. From Table 6 it is evident that that VOaccur and VO(cur)2 are a little more reactive than their ligand, cur. The presence of the central metal ion VO^{2+} has an observable effect on the antibacterial effect of cur.

2.4.2 | Minimum inhibitory concentrations

The concentration of test agent where no bacterial growth was detected was taken as the minimum inhibitory concentration (MIC). MICs of cur and NS as ligands and the corresponding VO complexes VOaccur, VOacNS, VO(cur)2 and VO(NS)2 against four bacterial strains were determined. The MICs of the studied materials and ampicillin as an antibacterial medication are summarized in Table 7. Ligand cur and its corresponding complexes VOaccur and VO(cur)2

TABLE 6 Effect of ligands and their corresponding VO complexes on Gram-negative and Gram-positive microorganisms

	Inhibition zone diameter (mm)			
	Gram-negative		>Gram-positive	
	E. coli	*P. aeruginosa*	*S. aureus*	*B. megaterium*
cur	13	11	14	15
NS	8	7	10	10
VOaccur	15	16	17	16
VOacNS	11	10	12	13
VO(NS)2	12	10	12	14
VO(cur)2	18	17	20	18
Tetracycline	21	20	22	20

TABLE 7 Minimum inhibitory concentration of ligands and corresponding VO complexes against Gram-negative and Gram-positive microorganisms

	MIC (μm)			
	E. coli	P. aeruginosa	S. aureus	B. megaterium
cur	30	25	30	30
NS	50	40	40	40
VOaccur	25	25	30	30
VOacNS	50	45	45	50
VO(NS)2	45	45	45	45
VO(cur)2	20	20	25	25
Tetracycline	15	15	20	20

have good inhibitory activity against all tested bacterial strains (MICs in the range of 20–30 μM). NS and its corresponding complexes VOacNS and VO(NS)2 show MICs in the range 40–50 μM. Hence, the molecular structure of the VO complexes has a marked effect on their antibacterial activity. The antibacterial activity of cur is improved by coordination to the oxovanadium ion.

2.4.3 | DNA affinity and DNA cleavage ability

The ability of cur and NS as ligands and the synthesized VO complexes VOaccur, VOacNS, VO(NS)2 and VO(cur)2 to cleave genomic DNA as one plausible mechanism of action was studied in parallel with that of controls utilizing agarose gel electrophoresis. They display DNA degradation effect in a concentration-dependent manner, which verifies their binding affinity to DNA (Figures 3 and 4). When the genomic DNA is permitted to interact with the ligands and their corresponding VO complexes at 1, 2 and 3 μM concentrations, the cleavage of DNA is found to increase

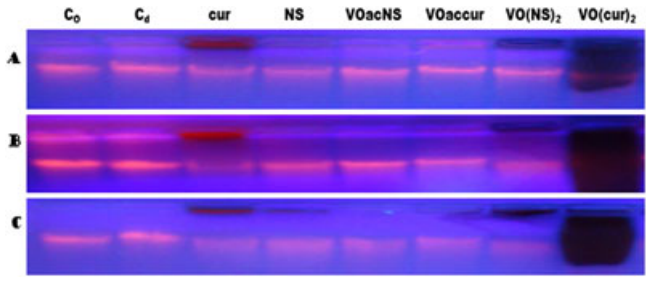


FIGURE 3 Degradation effect of 2 μM (A), 4 μM (B) and 6 μM (C) of ligands (NS and cur) and their corresponding VO complexes (lanes 3–8) on *E. coli* DNA. Lane 1: *E. coli* DNA; lane 2: *E. coli* DNA + DMSO

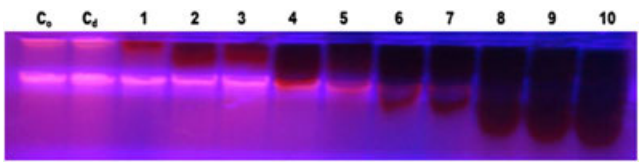


FIGURE 4 Degradation effect of 0.3–3 μM VO(cur)2 (lanes 3–12) on *E. coli* DNA. Lane 1: *E. coli* DNA; lane 2: *E. coli* DNA + DMSO

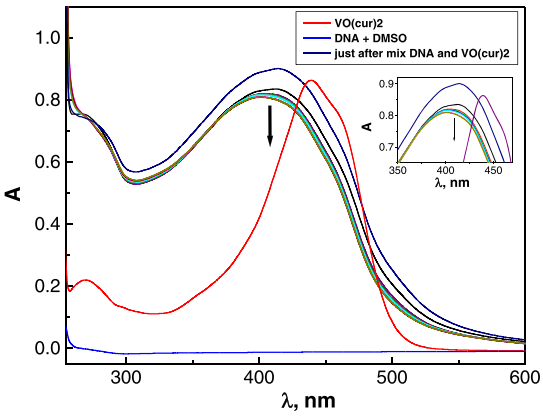


FIGURE 5 Electronic spectral scans of the interaction of DNA with VO(cur)2 in DMSO with interval time of 1 h at 37 °C

with increasing concentration of test complexes. The results indicate that VO(cur)2 complex has an efficient cleavage ability of DNA at 1 μM concentration (Figure 5). Furthermore, the ligands and the VO complexes demonstrate a considerable ability to cleave DNA at a concentration of 3 μM (Figure 3). VO(cur)2 displays a powerful degradation effect on DNA. Therefore, different concentrations of VO(cur)2 (0.3–3 μM) were applied to DNA (Figure 4). VO(cur)2 degrades DNA in concentration-dependent manner. The highest concentration of VO(cur)2 which is suitable for degrading completely 2 μg of DNA is 2.1 μM (Figure 5).

2.4.4 | Antioxidant activities

The formation of free radicals, reactive oxygen species (ROS), is unavoidable during the oxidative metabolic process. High cellular concentrations of these reactive molecules promote damage and denaturing reactions to many cellular components creating oxidative stress in cells thus resulting in many diseases including cancer.

2.4.4.1 | Superoxide dismutase (SOD) mimetic catalytic activity assay

Based on the DNA binding capability displayed so far by the tested ligands and their corresponding VO complexes, it was considered valuable to study their antioxidant activity. Superoxide radical anions ($O_2^{\bullet -}$) are sources for dynamic free radicals that have potential for reacting with biological macromolecules and thus causing cell damage. In this colorimetric-based assay, inhibition of the reduction of nitroblue tetrazolium (NBT) to formazan by the tested VO complexes was employed for detection of their SOD-mimetic superoxide scavenging catalytic activity. In the presence of $O_2^{\bullet -}$ and as the reaction proceeds, NBT is reduced to formazan, the colour changes from colourless to blue, with associated increase in the absorbance at 560 nm. SOD decreases the superoxide ion concentration and thereby lowers the rate of formazan formation. In the SOD-like activity test, the tested ligands

and their VO complexes compete with NBT for oxidation of the generated superoxide ions. The data presented in Table 8 indicates the scavenging efficacy of the ligands and the corresponding VO complexes, giving the final concentration that produces efficient quenching of the superoxide radical anion. VO(cur)2 and VOaccur and their ligand cur exhibit the highest antioxidant activities with inhibition of 61.4, 54.3 and 52.8%, respectively. The other VO complexes (VO(NS)2 and VOacNS) display SOD-like activity with inhibition lower than 50% (Table 8).

2.4.4.2 | 2,2′-Azino-bis(3-ethylbenzothiazoline-6-sulfonic acid) (ABTS) radical cation decolourization assay

The antioxidant activity evaluation adopted is based on the reduction in colour intensity of the free radical solution owing to scavenging of the free radical by the antioxidant material as determined colorimetrically at 734 nm. The evaluation employs the radical cation resulting from ABTS as a stable free radical. The benefit of ABTS-derived free radicals over other approaches is that the produced colour remains stable for more than 1 h and that the reaction is stoichiometric. The antioxidant activities of the ligands and the synthesized VO complexes were subjected to ABTS assessment. From the results obtained, it can be concluded that the antioxidant activities of VO(cur)2, VOaccur and cur are the highest in agreement with the SOD assay results. The other VO complexes exhibit lower than 50% inhibition of the ABTS radical cation (Fig. 6).

TABLE 8 SOD mimetic activity of ligands and their corresponding VO complexes as antioxidant agents

	Inhibition (%)
Control	—
Horse radish	69.4
cur	52.8
NS	37.1
VOaccur	54.3
VOacNS	41.8
VO(NS)2	48.5
VO(cur)2	61.4

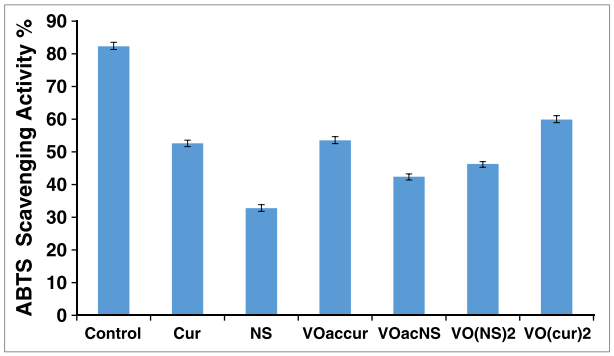


FIGURE 6 ABTS scavenging activity of t ligands (NS and cur) and their corresponding VO complexes (ligands and VO complexes: 2 μM)

2.4.4.3 | 2,2-Diphenyl-1-picrylhydrazyl (DPPH) radical scavenging activity

DPPH$^{\bullet}$ radical scavenging activity assessment is a standard process in antioxidant evaluation. In this study, the ability of the ligands and the synthesized VO complexes to interact with the stable DPPH free radical was measured to determine their radical scavenging activity. The tested ligands and the synthesized VO complexes show antiradical activity by inhibiting the formation of DPPH radicals where most of the test compounds display high to moderate DPPH$^{\bullet}$ interaction at 2 μM concentration (Figure 7). The highest antioxidant activity is noticed for the ligands and the synthesized VO complexes in the order of VO(cur)2 > VOaccur > cur > VO(NS)2 > VOacNS > NS, with comparable activity to that of vitamin C (standard) as represented in Figure 7. Antioxidant activity of the monocationic derivatives is related to their H$^{\bullet}$ radical donating capability to DPPH$^{\bullet}$ radical.

3 | EXPERIMENTAL

3.1 | Reagents and measurements

All required materials were purchased from Acrös and Sigma-Aldrich, and used directly without further purifications or treatment. Elemental analyses (C, H and N) were carried out with a GMBH VarioEl model V2.3 CHNS apparatus. Electronic spectra were recorded using 10 mm silica cells in a thermostatically controlled cell holder of a Jasco UV–visible spectrophotometer (model V-570). IR spectra (as KBr discs) were recorded with a Shimadzu FTIR-8101 Fourier transform IR spectrophotometer in the region 400–4000 cm^{-1}. Conductance measurements were carried out using a Jenway conductivity meter (model 4320), with an epoxy bodied conductivity cell (two electrodes, shiny) with cell constant calibration from 0.01 to 19.99 at 25 °C. Magnetic measurements of complexes were conducted with a Gouy

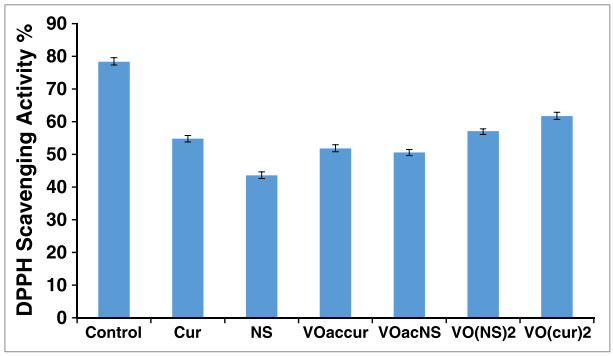


FIGURE 7 DPPH scavenging activity of ligands (NS and cur) and their corresponding VO complexes (ligands and VO complexes: 2 μM)

balance, and the diamagnetic correction was made by Pascal's contents and $Hg[Co(SCN)_4]$ as a calibrant. All synthetic reactions were carried out with magnetic stirring and held at the chosen temperature by immersion in a thermostatically controlled oil bath.

3.2 | Synthesis of *N*,*N*′-Bis(2-pyridyl)thiourea

N,*N*′-Bis(2-pyridyl)thiourea was prepared as reported previously,[24] by mixing 2-aminopyridine (19 g, 0.2 mol), carbon disulfide (6 ml, 0.1 mol) and triethylamine (15 ml, 0.1 mol) under reflux for 48 h. Excess carbon disulfide was removed under vacuum. The residue was diluted with 100 ml of water and cooled. Then the solid off-white needles of *N*,*N*′-bis(2-pyridyl)thiourea were collected, washed with water and dried in vacuum; m.p. 158 °C and yield 18 g (78%).

3.3 | Synthesis of VO complexes

3.3.1 | Synthesis of oxovanadium acetylacetonate curcumin complex (VOaccur)

Potassium hydroxide (0.056 g, 1 mmol) was added to a methanolic solution (15 ml) of curcumin (0.36 g, 1 mmol) with stirring until KOH was completely dissolved. The colour of the resulting solution changed gradually from dark yellow to deep red. The resulting solution was added carefully and very slowly dropwise to a methanolic solution (10 ml) of vanadyl acetalyacetonate (0.26 g, 1 mmol) to give a red precipitate. The reaction mixture was stirred for 3 h at 40 °C. The solvent was removed in vacuum and the residue was dissolved in dichloromethane. By filtration, the filtrate was brown in colour of the vanadium complex and dichloromethane was removed in vacuum. The complex was recrystallized from a hot solution of dichloromethane affording fine green powder in 61% yield.

3.3.2 | Synthesis of oxovanadium acetylacetonate *N*,*N*′-(2-pyridyl)thiourea complex (VOacNS)

A suspended methanolic solution (10 ml) of *N*,*N*′-(2-pyridyl) thiourea (0.23 g, 1 mmol) was added carefully and very slowly dropwise to vanadyl acetylacetonate (0.26 g, 1 mmol) in 10 ml of methanol at room temperature. No change in colour was observed after addition (pale green). The resulting solution was heated for 3 h at 40 °C. The colour changed to brownish green with no formation of precipitate in the reaction medium. Methanol was removed in vacuum. The residue was recrystallized from hot methanol to afford a brownish green powder in 72% yield.

3.3.3 | Synthesis of oxovanadium bis-*N*,*N*′-(2-pyridyl)-thiourea complex (VO(NS)2)

Vanadyl acetylacetonate (0.26 g, 1 mmol) in 10 ml of methanol was added dropwise to a suspended methanolic solution (10 ml) of *N*,*N*′-(2-pyridyl)thiourea (0.46 g, 2 mmol) and KOH (0.056 g, 1 mmol) at room temperature. No change in colour was observed after addition (pale green). The resulting reaction mixture was heated under stirring at 50 °C for 5 h affording a change in colour to brown with no observation of precipitation. The solvent was removed in vacuum and the residue was washed with water and recrystallized from hot methanol, affording a brownish green powder in 80% yield.

3.3.4 | Synthesis of oxovanadium bis-curcumin complex (VO(cur)2)

Synthesis of VO(cur)2 has already been reported by Thompson *et al.*[17] as follows. Vanadyl acetylacetonate (0.26 g, 1 mmol) in 10 ml of methanol was added dropwise to a methanolic solution (10 ml) of curcumin (0.72 g, 2 mmol) at room temperature. No change in colour was observed after addition (pale green). The resulting reaction mixture was heated under stirring at 50 °C for 5 h affording a deep red precipitate. The solvent was removed in vacuum and the residue was washed with methanol and recrystallized from hot methanol, affording a deep red product in 75% yield.

All the characteristic data for the studied complexes are collected in Tables 1–3. The stoichiometry of the VO complexes was determined using the continuous variation method and presented in Figures S1 and S2. The thermogravimetric parameters of the VO complexes were calculated from the spectrophotometric measurements according to the continuous variation method and are collected in Table 4.

3.4 | Catalytic procedure

The catalytic oxidation of 1-octene (1.0 mmol) was carried out with 30% aqueous H_2O_2 as the oxygen source (3.0 mmol) using VO complexes as catalysts (0.02 mmol) in acetonitrile (10 ml) at 50 °C for 16 h under homogeneous aerobic atmosphere. The reaction products were analysed by a Shimadzu GC–MS model QP2010 SE equipped with Rxi-5 Sil MS capillary column (30 m length × 0.25 mm ID × 025 μm film thickness). The analysis was performed using the following GC parameters: injector temperature, 250 °C; initial oven temperature, 40 °C (held for 1 min), increased to 200 °C at a rate of 10 °C min^{-1}. The total time required for one GC run was 17 min. The inlet was operated in the splitless mode. The MS transfer line was kept at 200 °C. High-purity helium was used as carrier gas with a flow rate 1 ml min^{-1}. LabSolution software was used to control the system and to acquire the analytical data. All the catalytic oxidation product percentages are collected in Table 5.

3.5 | Antibacterial activities

The antimicrobial study of the ligands and their corresponding VO complexes was carried out via the cup diffusion method.[38] The antibacterial assessment was performed against typical bacterial strains of Gram-negative *E. coli* ATCC 25922 and *P. aeruginosa* ATCC 27853 and Gram-

positive *S. aureus* ATCC 25923 and *B. megaterium* ATCC 14591. The tested ligands and VO complexes were dissolved in DMSO at a concentration of 20 μM. Luria–Bertani agar (LBA) medium was made for inoculation and bacterial growth as described by Youssef *et al.*[39] An aliquot of solution of the ligands and synthesized VO complexes equivalent to 100 μM was placed separately in the agar. The LBA plates were kept for 24 h at 37 °C and the resulting inhibition diameter zones were measured. The antimicrobial activities of ligands and the synthesized VO complexes against Gram-positive and Gram-negative bacteria were evaluated (Table 6).

3.6 | Minimum inhibitory concentrations

Determination of MICs of the studied VO complexes was made according to the standard CLSI/NCCLS procedure.[40] Four bacterial strains representing two Gram-negative and two Gram-positive species were used for this experiment. A typical methodology, recently described[41] in brief, involved DMSO solutions of the VO complexes being used as test agents in various concentrations (0.5–50 μM). MIC values are the average of triplicate runs (Table 7).

3.7 | Nuclease-like activity assay

DNA cleavage assay of the tested VO complexes was carried out as described previously.[41] In brief, the VO complexes were dissolved in DMSO (10 mM) and 1, 2 and 3 μM added individually to 2 μg of *E. coli* DNA. The DNA only and DNA with DMSO were used as controls. The reactions were performed at 37 °C for 1 h. A solution of 0.06% (*w*/*v*) bromophenol blue, 10% (w/v) ficol 400 and 0.5% (w/v) sodium dodecylsulfate was added to the reaction mixtures proir to running the gel. DNA degradation was evaluated via agarose gels electrophoresis.[42]

3.8 | Antioxidant activity

3.8.1 | SOD mimetic catalytic activity assay

SOD mimetic catalytic activity of the synthesized VO complexes was evaluated using NBT/NADH/PMS (nitroblue tetrazolium/reduced nicotinamide/phenazine methosulfate) to photogenerate a reproducible and constant flux of $O_2^{\bullet-}$ in phosphate buffer (pH = 8.3).[43] A typical methodology has been recently described[41] in brief, where herein the ligands or VO complexes (2 μM) were used as test compounds. The SOD mimetic catalytic activity data are the average of triplicate experiments.

3.8.2 | ABTS radical cation decolourization assay

ABTS forms a relatively steady free radical, which decolorizes in its non-radical form. The evaluation of ABTS free radical scavenging activity was assessed spectrophotometrically.[44] A typical methodology has been recently described in brief[41] and herein the current VO complexes (2 μM) were used as test compounds. The ABTS radical cation data are the average of triplicate experiments.

3.8.3 | Estimation of antioxidant activities using DPPH

Radical scavenging activity of cur and NS, and their VO complexes against stable DPPH was evaluated spectrophotometrically. When DPPH reacts with an antioxidant compound, which gives hydrogen, it is reduced. Radical scavenging activity of the ligands and their corresponding VO complexes (2 μM) was measured according to a reported method.[45] Determination of antioxidant activities of each of the ligands and VO complexes using DPPH was carried out as triplicates. The percentage of antioxidant activity was determined using the following formula: % antioxidant activity =100 − (sample absorbance − blank absorbance) × 100 (Table 8).

4 | CONCLUSIONS

Four binary and ternary mono-oxovanadium(IV) complexes of ac, cur and NS were synthesized. They were characterized using elemental analysis, IR and UV–visible spectroscopies and conductivity and magnetic measurements. In the complexes, cur and NS act as bidentate ligands through O-atoms, and N- and S-atoms, respectively. The spectrophotometric continuous variation method was used to calculate the formation constants K_f of the VO complexes. The oxidation of 1-octene by aqueous H_2O_2 as external oxidant in acetonitrile catalysed by the VO complexes afforded various oxidation products with high conversion and low chemoselectivity to the epoxy product. The catalytic potential of the VO complexes depends upon their electronic and steric properties. VO(cur)2 with the highest steric demand and electronic effect shows the highest catalytic activity; conversely, VOacNS with the least steric and electronic effects is less active. The catalytic results are in agreement with the formation constants K_f of the current complexes. The VO complexes exhibit good antibacterial and antimicrobial activities. The antioxidant activity of the VO complexes and their ligands has been studied. The VO complexes exhibit high DNA affinity and DNA cleavage ability which have been followed using visible spectroscopy. The antibacterial activities of cur and its complexes are an important issue because these compounds can be used as medication as antibiotics to inhibit bacterial growth. The ROS in a cellular system can attack DNA or proteins in the cells. So, the removal of these ROS is important for living organisms. Curcumin and its complexes can be used as antioxidants to scavenge the ROS. The compounds that degrade DNA can be used as anticancer agents.

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