



Research Article

ISSN : 0975-7384
CODEN(USA) : JCPRC5

Synthesis of Biological Active N₂O₂ Type of Novel Schiff Base Metal Complexes Derived from 4-Amino Antipyrine Using Tea

SD Dakore* and VT Kamble

Organic Chemistry Research Laboratory, School of Chemical Sciences, Swami Ramanand Teerth Marathwada University, Vishnupuri, Nanded, India

ABSTRACT

New Schiff base complexes of Cu (II), Co (II), Ni (II) and Zn (II) have been synthesized. Schiff bases synthesized from 4-amino antipyrine, 2- thiophene carboxaldehyde & acetyl acetone in first step. In second step metal complexes are prepared from synthesized schiff base and divalent metal ions. In both the steps silica supported tri ethylamine catalyst is used at room temperature. The complexes were characterized by IR, ¹H NMR, EPR spectro, magnetic moments, conductance, thermal analysis (TGA & DTA), and powder x-ray analysis (XRD). The antimicrobial studies of these complexes against staphylococcus typhi, staphylococcus aureus, Escherichia coli, Bacillus subtilis species by minimum inhibitory consent ratio (MIC) method revealed that these complexes possess potent antibacterial activity.

Keywords: 2-Thiophene carboxaldehyde; 4-Amino antipyrine; Acetyl acetone; Divalent metal ions; Schiff basecomplex

INTRODUCTION

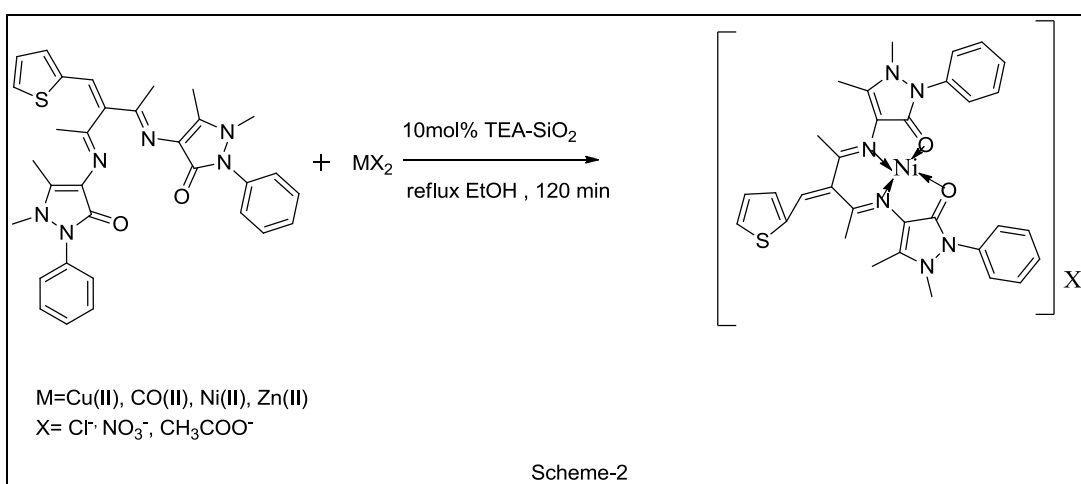
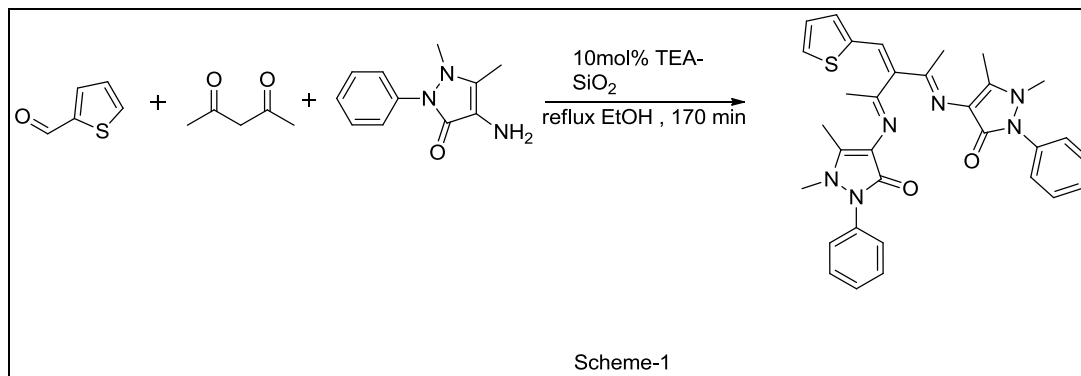
Large number of co-ordination compounds has applications in different fields [1-3]. Schiff bases itself have some antimicrobial activity which have been increased by forming complexes with metals [4]. The transition metal complexes of 4-aminoantipyrine have importance in the field chemistry due to their wide applications in like pharmacological, therapeutical, biological, industrial, analytical area[5-13].Schiff Base complexes of 4-aminoantipyrine has antifungal, antibacterial, analgesics, sedative, antipyretic and anti inflammatory activity [14,15]. Now a days many research papers have been reported on transition metal complexes derived from 4-aminoantipyrine with aza or aza - oxo donar atoms [16-19]. Because of their interesting structural features a wide range of metal complexes derived from antipyrine derivatives have been reported. Complexes of 4-aminoantipyrine are also has great variety of applications in area of catalysis. The synthetic protocol for preparation of metal complexes derived from 4-aminoantipyrine, heterocyclic aldehydes & acetyl acetone involved in three different steps. Herein, we report new method to synthesize metal complexes of schiff bases having three components only into two steps. The aim of the present work is also to synthesize and characterize Co(II), Cu(II), Zn(II), Ni(II) metal complexes with newly synthesised schiff base ligand derived from 4-amino antipyrine , 2-thiophene carboxaldehyde and acetyl acetone.

EXPERIMENTAL SECTION

Material and methods

IR spectra (400–4000 cm⁻¹) were recorded on Shimadzu FTIR spectrophotometer using KBr discs and the absorption bands are expressed in cm⁻¹. ¹H NMR spectra were recorded in DMSO-d₆ with tetramethyl silane as an internal standard. Molar conductivity of 10⁻³ M solution in DMSO was obtained on C- 100 Elico digital conductivity meter at room temperature. Magnetic susceptibilities were recorded on Guoy balance using AR grade CuSO₄ and FeSO₄ as standard. EPR spectra of complexes are performed in solid state at room temperature on Varian-E-4X band EPR spectrophotometer. TG/DTA scans were recorded on Mettler-Toledo-851 TGA-DTA instrument at linear heating rate of 100 per minute under nitrogen atmosphere in a temperature range 25-1000°C.

X-ray powder diffraction patterns of complexes were recorded in the 2θ range of 10-800 on Bruker X-D-8 advanced diffractometer and XRD scans with the help of powder X-programme. Analytical grade chemicals brought from Sigma-Aldrich, INC. were used throughout this work.



Typical procedure

Synthesis of Schiff base:

A mixture of acetyl acetone (10mmol), 4-aminoantipyrine (20mmol) and 2-thiophene carboxaldehyde (10mmol) along with 10 mol % solid supported triethylamine in ethanol (50 ml) on water bath was refluxed until completion of the reaction. The completion of the reaction was monitored by thin layer chromatography (TLC). After completion of the reaction, the catalyst was filtered, washed with ethanol and the filtrate was concentrated under reduced pressure. The crude product was purified by recrystallisation with hot ethanol. The recovered catalyst was activated at 180°C for 2 hr & reused four times for the preparation of complexes.

Synthesis of metal complexes:

A mixture of schiff base ligand (2mmol) and metal salt (2mmol) along with 10 mol% solid supported tri ethyl amine in ethanol (15 ml) was refluxed for 1hr. The resulting colored complex along with insoluble catalyst was filtered; washed with ethanol, acetone and petroleum ether. Then metal complex was dissolved in DMSO (2x15ml) to separate the catalyst and then filtered. The filtrate was then concentrated under reduced pressure to afford shiny colored complex which was dried over calcium chloride (65 % yield).

RESULT AND DISCUSSION

Novel schiff base complexes of N₂O₂ type have been synthesized by non template method utilizing solid supported tri ethyl amine catalyst as a catalyst. The investigated complexes were characterized and evaluated for their antimicrobial activity against four bacterial stains. The analytical data suggest the formula of complexes as [ML₁] X₂ where M = Co(II), Ni(II), Cu(II), Zn(II) & X = Cl⁻, NO₃⁻ & CH₃COO⁻. Conductivity measurements in DMSO indicate them to be electrolytic in nature (40-60 ohm⁻¹cm²mol⁻¹). The melting point of all complexes was above 250°C and all complexes are intensively colored. Magnetic moment values suggest square planar environment around metals.

Table 1: Analytical data of $[M(C_{32}H_{32}N_6O_2S)]X_2$

S No	Mol. Formula of Complex	Mol. Wt.	Colour	Melting Point	% C	% H	% N	$\lambda M \text{ ohm}^{-1} \text{ cm}^2 \text{ mol}^{-1}$	M.M B.M
1	$[\text{Cu}(\text{C}_{32}\text{H}_{32}\text{N}_6\text{O}_2\text{S})] \text{Cl}_2$	699.15	Blue	227	54.97 (54.65)	4.61 (4.52)	12.02 (12.36)	11	1.72
2	$[\text{Cu}(\text{C}_{32}\text{H}_{32}\text{N}_6\text{O}_2\text{S})](\text{NO}_3)_2$	751.54	Dark Blue	231	51.09 (51.50)	4.29 (4.62)	14.90 (15.10)	9	1.72
3	$[\text{Cu}(\text{C}_{32}\text{H}_{32}\text{N}_6\text{O}_2\text{S})(\text{CH}_3\text{Coo})_2]$	746.33	Blue	229	57.93 (57.58)	5.13 (5.25)	11.26 (11.33)	13	1.72
4	$[\text{Co}(\text{C}_{32}\text{H}_{32}\text{N}_6\text{O}_2\text{S})] \text{Cl}_2$	694.54	Brown	237	55.35 (55.50)	4.64 (4.32)	12.10 (12.35)	8	2.82
5	$[\text{Co}(\text{C}_{32}\text{H}_{32}\text{N}_6\text{O}_2\text{S})(\text{NO}_3)_2]$	747.64	Dark Brown	233	51.41 (51.48)	4.31 (4.35)	14.99 (15.01)	15	2.85
6	$[\text{Co}(\text{C}_{32}\text{H}_{32}\text{N}_6\text{O}_2\text{S})(\text{CH}_3\text{Coo})_2]$	741.72	Black	240	58.29 (58.90)	5.16 (5.54)	11.33 (11.64)	14	2.87
7	$[\text{Ni}(\text{C}_{32}\text{H}_{32}\text{N}_6\text{O}_2\text{S})] \text{Cl}_2$	694.3	Light Green	241	55.36 (55.08)	4.65 (4.01)	12.10 (12.40)	12	-
8	$[\text{Ni}(\text{C}_{32}\text{H}_{32}\text{N}_6\text{O}_2\text{S})(\text{NO}_3)_2]$	747.4	Green	247	51.42 (51.12)	4.32 (4.09)	14.99 (15.20)	7	-
9	$[\text{Ni}(\text{C}_{32}\text{H}_{32}\text{N}_6\text{O}_2\text{S})(\text{CH}_3\text{Coo})_2]$	741.48	Green	250	58.31 (57.97)	5.17 (4.83)	11.33 (12.03)	9	-
10	$[\text{Zn}(\text{C}_{32}\text{H}_{32}\text{N}_6\text{O}_2\text{S})] \text{Cl}_2$	698.1	Buff	246	54.83 (55.10)	4.60 (4.90)	11.99 (12.30)	12	-
11	$[\text{Zn}(\text{C}_{32}\text{H}_{32}\text{N}_6\text{O}_2\text{S})(\text{NO}_3)_2]$	754.1	Buff	255	50.97 (51.12)	4.28 (4.42)	14.86 (14.35)	12	-
12	$[\text{Zn}(\text{C}_{32}\text{H}_{32}\text{N}_6\text{O}_2\text{S})(\text{CH}_3\text{Coo})_2]$	748.18	Buff	253	57.79 (58.04)	5.12 (5.26)	11.23 (11.77)	14	-

IR spectra

The IR spectra of schiff base ligands showed the absence of -C=O group in aldehyde and ketones. As well as they showed absence of amino stretching in antipyrine compounds. The presence of imine stretching frequency between $1575\text{-}1600 \text{ cm}^{-1}$ showed the confirmation of formation of schiff bases ligands. The remaining -C=O group of antipyrine showed $1640\text{-}1650 \text{ cm}^{-1}$ stretching frequencies. The metal-nitrogen and metal-oxygen bonds showed the 516 cm^{-1} and 447 cm^{-1} frequencies respectively.

NMR spectra

The NMR spectrum of the all the metal complexes exhibits a singlet at δ 2.35-2.42 ppm of C-CH_3 , singlet at δ 3.05-3.11 ppm of N-CH_3 and singlet at δ 2.85-2.92 ppm of -N=C-CH_3 regions which showed the formation and confirmation of the metal complexes. The remaining aromatic protons are appeared at expected region.

EPR spectra

The EPR spectra of the $[\text{Ni}(\text{C}_{32}\text{H}_{32}\text{N}_6\text{O}_2\text{S})(\text{NO}_3)_2]$ complex in powder form at room temperature shows isotropic signals with $g_{\parallel} = 1.9973$, $g_{\perp} = 1.9945$, and $g_{\text{iso}} = 1.9955$, $A_{\parallel} = 16.66 \text{ G}$, $A_{\perp} = 25 \text{ G}$ and exchange coupling interaction constant $G = 0.6846$. This finding indicates that the observed 'g' values for the complex are less than 2.3 in agreement with the covalent character of the metal ligand bond. The trend $g_{\parallel} > g_{\perp} > 2.0023$ observed for the Ni(II) complexes indicates that unpaired electron is localized in the $\text{dx}^2\text{-y}^2$ orbital.

Powder X-ray analysis

Powder XRD diffractogram of Co(II) complexes were recorded in the range $20\text{-}80^\circ$ at wavelength 1.5447° \AA . The diffractogram and associated data depict the 2θ value for each peak, relative intensity and inter-planar spacing (d values). Major reflexes were used to determined corresponding interplanar distances. The X-ray diffraction pattern of Co(II) complexes with respect to major peaks having relative intensity greater than 10% has been indexed by using computer programme. Miller indices (hkl), unit cell parameters and unit cell volume were also obtained from above indexing method. The unit cell of Co(II) complex yielded values of lattice constants $a = 18.2147$, $b = 13.4867$, $c = 3.9121$ and unit cell volume 867.210 \AA^3 . Also, in association with these cell parameters, the conditions such as $a \neq b \neq c$ and $\alpha = \beta = \gamma = 90^\circ$ required for sample to be orthorhombic were tested and found satisfactory. In conclusion the complexes Co(II) have orthorhombic crystal system. The experimental density values of complexes were determined using specific gravity method and found to be 0.7732 g cm^{-3} for the Co(II) complex.

Using the experimental density values, the molecular weight of the complexes (M), Avogadro's number (N), and the volume of unit cell (V), the number of molecules per unit cell (n), were calculated using the equation $\rho = nM/NV$ and they were found to be one. With these values, the theoretical densities were computed and found to be 0.7787 g cm^{-3} for respective complexes. Comparison of experimental and theoretical density value shows good agreement within the limits.

Thermal analysis

On TG curve of $[\text{Co}(\text{C}_{32}\text{H}_{32}\text{N}_6\text{O}_2)(\text{NO}_3)_2]$ complex, mass loss of 8.15% (calcd. 8.12%) in the range 30-240°C indicating the removal of non-coordinated nitrate. An endothermic peak on DTA curve at 160°C also corresponds to loss of nitrate. The second step of the decomposition between 250-320°C with 58.01% mass loss (calcul. 58.20%) is attributed to the removal of the coordinated nitrate and organic moiety of the complex. The third step, from 320 to 550°C indicating removal of remaining part of coordinated ligand. For this a broad exothermic peak was at 510°C observed in DTA. The mass loss continued with slow decomposition of the remaining part up to 800°C corresponding to final residue of cobalt oxide. Amount of cobalt oxide found in residue is close agreement with calculated.

Kinetic data

The kinetic and thermodynamic parameters viz, order of reaction (n), energy of activation (Ea), three exponential factor (Z) etc. for non-isothermal decomposition of metal complexes were determined by the Horowitz-Metzar approximation method. The data obtained are given in table 4. The calculated values of the activation energy of the complexes are relatively low, indicating the autocatalytic effect of the metal ion on the thermal decomposition of the complex. The negative activation entropy values suggest that the activated complex were more ordered than the reactants and that the reaction were slow. The more ordered nature may be due to polarization of bonds in activated state.

Antimicrobial activity

The *in vitro* antibacterial activities of synthesized complexes have been studied by disc diffusion method. The antibacterial activities were done at 100 µg/ml concentrations in DMF solvent using method four bacterial strains (*S.typhi*, *S. aureus*, *E. coli* and *B. subtilis*) by the minimum inhibitory concentration (MIC). These bacterial strains were incubated for 72 h at 27°C. Standard antibacterial (Cefodox and Linazoid) were used for comparison under similar conditions. Activity was determined by measuring the diameter of the zone of inhibition (mm). The data of antibacterial activities tabulated in Table 5 indicated that Zn(II) and Cu(II) complexes are more active against the bacterial strains *S. coli* and *S.typhi* as compared to other bacterial strains. Cu (II) and Zn (II) complexes were found to be moderately active against all bacterial strains.

Table 2: EPR parameters for metal complexes

Compound	Gyrometric ratio G	A gauss	G	e/gm*10 ²¹
$[\text{Ni}(\text{C}_{32}\text{H}_{32}\text{N}_6\text{O}_2\text{S})(\text{NO}_3)_2]$	$g_{\parallel} = 1.9973$ $g_{\perp} = 1.9945$ $g_{\text{av}} = 1.9955$	$A_{\parallel} = 16.66$ $A_{\perp} = 25$	0.6846	1.5047

Table 3: Millar indices and interplaner distances

Complex	h k l	2θ observed	2θ observed	D
$[\text{Co}(\text{C}_{32}\text{H}_{32}\text{N}_6\text{O}_2\text{S})(\text{NO}_3)_2]$	0 1 0	6.577	6.567	12.8886
	0 2 0	13.176	13.156	5.169
	1 2 0	14.046	15.492	3.9499
	4 0 0	19.502	20.211	2.9443
	0 0 1	22.744	23.738	2.6539
	1 1 1	24.167	27.244	2.1381

Table 4: Thermal decomposition and kinetic parameters

Complex	DTA pea K °C	Temp. range °C	Mass loss(%) observed (calculated)	Nature of Decomposition	Order of reaction	ΔE kg/mole	Δs JK/Mole	GKJ/Moles	Frequency factor Z
$[\text{Co}(\text{C}_{32}\text{H}_{32}\text{N}_6\text{O}_2\text{S})(\text{NO}_3)_2]$	160	0-240	8.15 -8.12	NO ₃	1.9	6.977	-276.292	21.161	3.211x10 ⁻²
	260	250- 470	58.01 -58.2	NO ₃ -& Ligand	1.9	11.195	-252.667	27.617	7.306x10 ⁻¹
	510	470- 550	33.84 -33.68	ligand	1.9	27.213	-224.667	43.319	2.296x10 ⁻¹

Table 5: Antibacterial activity of complexes of type $[M(C_{32}H_{32}N_6O_2S)X_2]$

Sr. No.	Complex	<i>S. typhi</i>	<i>S. aureus</i>	<i>E. coli</i>	<i>B. subtilis</i>
1	$[Cu(C_{32}H_{32}N_6O_2S)] Cl_2$	7.3	5.2	6.8	5.1
2	$[Cu(C_{32}H_{32}N_6O_2S)](NO_3)_2$	6.7	5.3	6.7	5.5
3	$[Cu(C_{32}H_{32}N_6O_2S)](CH_3COO)_2$	7.1	5.5	5.7	5.8
4	$[Co(C_{32}H_{32}N_6O_2S)] Cl_2$	5.9	5.4	5.8	5.1
5	$[Co(C_{32}H_{32}N_6O_2S)](NO_3)_2$	5.6	4.9	5.5	5.3
6	$[Co(C_{32}H_{32}N_6O_2S)](CH_3COO)_2$	6.1	4.6	7	5.4
7	$[Ni(C_{32}H_{32}N_6O_2S)] Cl_2$	6.7	6.1	4.7	4.3
8	$[Ni(C_{32}H_{32}N_6O_2S)](NO_3)_2$	5.8	6.2	5.9	4.7
9	$[Ni(C_{32}H_{32}N_6O_2S)](CH_3COO)_2$	7.2	6.2	6.6	4.1
10	$[Zn(C_{32}H_{32}N_6O_2S)] Cl_2$	6.6	4.1	4.9	5.3
11	$[Zn(C_{32}H_{32}N_6O_2S)](NO_3)_2$	5.9	5.2	6.2	5.7
12	$[Zn(C_{32}H_{32}N_6O_2S)](NO_3)_2$	4.5	4.7	6.1	5.9
13	Cefodox	7.4	7.5	7.4	6.9
14	Linazoid	7.9	6.9	7.9	7.3

CONCLUSION

In summary, we have synthesized new schiff base ligand complexes of Cu (II), Co (II), Ni (II) and Zn (II). The Schiff base ligands are prepared from 4-amino antipyrine, 2- thiophene carboxaldehyde & acetyl acetone using tri ethylamine catalyst is used at room temperature. The complexes were characterized by IR, 1H NMR, EPR spectro, magnetic moments, conductance, thermal analysis (TGA & DTA), and powder x-ray analysis (XRD). Schiff base ligand complexes of transition metal ions were observed as tetradentate in nature. Metal complexes decompose above $250^\circ C$ suggesting good thermal stability. Molar conductivity of complexes in DMSO showed 1:2 electrolytic natures. Magnetic moment suggest square planar environment around metal ion. Thermal analysis of complexes gives the information regarding decomposition pattern of metal ligand ratio. Finally, the above observations it is showed that schiff base ligand complexes has undergone structural rearrangement to acquire stability and co-ordinated to metal through free donar atoms. The antimicrobial activity showed that Cu (II) and Zn (II) complexes were found to be moderately active against all bacterial strains.

REFERENCES

- [1] S. Kumar, D.N.Dhar and P.N. Saxena. *J. Sci. Indus. Res* **2009**, 68: 181.
- [2] H.C. Aspinall, 2002 *Chem. Rev.* 102: 1807.
- [3] K.L. Haas and K.J. Franz. *Chem. Rev.* **2009**, 109: 4921.
- [4] Raman, N.Raja, J.D. Sakthivel. *Molecules*, 2006, 11: 904-914.
- [5] KZ Ismail, A El-Dissouky, and Shehada AZ **1997**, 16: 2909 – 2916.
- [6] Singh L, Sharma A., and Sindhu S.K., *Asian J.Chem.* **1999**, 11: 1445-1450.
- [7] G Shankar, PR Premkumar. and Ramalingam S.K. *Polyhedron* **1986**, 15: 991-994.
- [8] Chopra JR., Uppal D, Arrora U.S. and Gupta S. *Asian J. Chem.* 2000, 12: 1277-1281
- [9] JS.Cunha, S.M. Oliveira, M.T. Rodrigues, R.M. Bastos J. Ferrari, C.M.A.De Oliveira, L.Kato, H.B. Napolitano, I.Vencato, C.Lariucci, *J.Mol. Stru.* **2005**, 752: 32-39.
- [10] Raman N, Mitu L. Sakthivel A. and pandi M.S.S.J. *Iran Chem. Soc.*, **2009**, 9: 738 – 748.
- [11] YY. Liu, H. Wang and F.Li, *J. Molecules* **2013**, 18: 877-893.
- [12] Cunha S, Oliveira, S.M. Rodrigues, Jr MT, Bastos, R.M. Ferrari, d Oliveria, C.M.A. kato L, Na politano, *J. Mol. Struct.* **2005**, 752, 32-39.
- [13] Gilman AG, Goodman L.S, Gilman A. *Macmillan publishing Co*, New York, USA.
- [14] C Sulekh, J Deepali, S Amit kumar, S Pratibha. *Molecules* **2009**, 14, 174-190.
- [15] J Joseph, K. Nagashri, G-Ayisha Bibin Rani. *J. Saudi Chem. Soci.* **2013**, 17, 285-294.
- [16] Deepa K., Madhu N.T., Radhakrishnan PK. *Synth. React. Inorg. Met. Org. Nano-Met Chem.* **2005**, 35, 883-888.
- [17] RK Agrawal, B Prakash. *Trans. Met. Chem.* **2005**, 30, 696-705.
- [18] B Anupama, C.G. kumari *Research journal of pharmaceutical, biological and chemical sciences* **2011**(4) 140-159
- [19] H Abbas and WJJ Jawad *J. of applicable chemistry* **2013**, 2(3), 438-446