



Synthesis, Structure and Antioxidant Properties of Nickel(II) Complex with *bis*(Benzimidazol-2-ylmethyl)allylamine

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Received: 14 March 2014;

Accepted: 16 May 2014;

Published online: 17 March 2015;

AJC-16939

A complex of nickel(II) picrate (pic) with *bis*(benzimidazol-2-ylmethyl)allylamine (AIDB), with composition $[\text{Ni}(\text{AIDB})_2(\text{pic})_2]$, was synthesized in high yields and characterized by elemental analyses, molar conductivities, UV-visible spectra and IR spectra. X-ray crystallographic investigation of Ni(II) complex is distorted octahedral coordination geometry. The antioxidant activity of the complex was determined by the superoxide and hydroxyl radical scavenging methods *in vitro*, which indicate that it is a scavenger for OH^\bullet and O_2^\bullet radicals.

Keywords: *bis*(Benzimidazol-2-ylmethyl)allylamine, Crystal structure, Nickel(II) complex, Antioxidant activity.

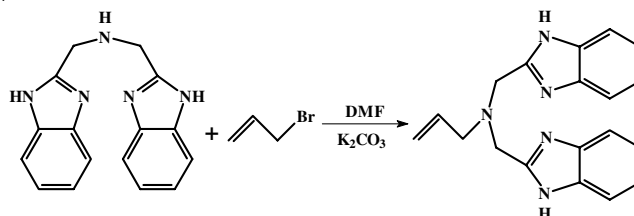
INTRODUCTION

Benzimidazole plays an important role, aimed at developing new antimicrobial agents with new mechanism of action. Literature survey reveals benzimidazole showed excellent antimycobacterial properties¹. Benzimidazole and its derivatives are reported to be physiologically and pharmacologically active and find applications in the treatment of several diseases like epilepsy, diabetes². It is an important pharmacophore and privileged structure in medicinal chemistry encompassing a diverse range of biological activities including antihistamine^{3,4}, antiulcerative⁵, antiproliferative^{6,7}, antitumor^{8,9}, antikinase^{10,11}, activities¹², cytotoxicity¹³. In this contribution, the synthesis, characterization and antioxidant properties of Ni(II) complex with *bis*(benzimidazol-2-ylmethyl)allylamine (AIDB) are presented.

EXPERIMENTAL

All chemicals used were of analytical grade. C, H and N contents were determined using a Carlo Erba 106 elemental analyzer. The IR spectra were recorded in the 4000-400 cm^{-1} region with a Nicolet FT-VERTEX 70 spectrophotometer using KBr pellets. Electronic spectra were taken on Lab-Tech UV Bluestar and Spectrumlab 722sp spectrophotometers. ¹H NMR spectra were obtained with a Mercury plus 400 MHz NMR spectrometer with TMS as internal standard and CDCl_3 as solvent. The fluorescence spectra were performed on a LS-45 spectrofluorophotometer at room temperature. The antioxidant activity was performed in DMF solution with a 722-SP spectrophotometer.

Preparation of *bis*(benzimidazol-2-ylmethyl)allylamine (AIDB): 4.432 g (0.016 mol) *bis*(benzimidazol-2-ylmethyl)amine¹⁴ mixed with 2.322 g (0.019 mol) allyl bromide in 40 mL DMF and refluxed for 12 h. The brownish liquid was filtered. Yellow precipitate was produced by washing with distilled water and recrystallized from MeOH (**Scheme-I**). Yield 4.03 g (79.4 %). Anal. Calcd. for $\text{C}_{18}\text{H}_{19}\text{N}_5$ (%): C, 63.43; H, 5.62; N, 20.55; found (%): C, 63.49; H, 5.59; N, 20.64. Selected IR data (KBr, ν_{max} , cm^{-1}): 1600 $\nu_{(\text{C}=\text{C})}$, 1445 $\nu_{(\text{C}=\text{N})}$, 1272 $\nu_{(\text{C}-\text{N})}$. ¹H NMR (400 MHz, CDCl_3): 7.2-7.68 (m, 8H, benzimidazole), 5.11-5.92 (m, 5H, $-\text{CH}_2-\text{CH}=\text{CH}_2$), 4.09 (s, 4H, $\text{N}-\text{CH}_2$). Λ_{M} (DMF, 297 K): 0.8 $\text{S cm}^2 \text{mol}^{-1}$. UV/visible (DMF): $\lambda = 277 \text{ nm}$.



Scheme-I: Synthesis of the ligand AIDB

Preparation of $[\text{Ni}(\text{AIDB})_2(\text{pic})_2]$: To a stirred solution of AIDB (0.0316 g, 0.1 mmol) in hot MeOH (3 mL) was added $\text{Ni}(\text{pic})_2$ (0.0145 g, 0.05 mmol) in MeOH (4 mL). A pale-yellow crystalline product formed rapidly. The precipitate was filtered off, washed with MeOH and absolute Et_2O and dried *in vacuo*. The dried precipitate was dissolved in DMF to form a yellow solution into which Et_2O was allowed to diffuse at room temperature. Pale yellow crystals of $[\text{Ni}(\text{AIDB})_2](\text{pic})_2$

suitable for X-ray diffraction were obtained after five days. Yield 0.027 g (85.4 %). Anal. Calcd. for $C_{50}H_{42}N_{16}O_{14}Ni$ (%): C, 44.53; H, 2.64; N, 19.09; Cd, 3.20; found: C, 44.48; H, 2.69; N, 19.17; Cd, 3.14. Selected IR data (KBr, ν_{max} , cm^{-1}): 1633 $\nu_{(C=C)}$, 1495 $\nu_{(C=N)}$, 1312 $\nu_{(C-N)}$. Λ_M (DMF, 297 K): 47.2 $S\ cm^2\ mol^{-1}$. UV/visible (DMF): $\lambda = 274, 380\ nm$.

X-ray structure determination: A suitable single crystal was mounted on a glass fiber and the intensity data were collected on a Bruker Smart CCD diffractometer with graphite-monochromatized MoK_{α} radiation ($\lambda = 0.71073\ \text{\AA}$) at 296 K. Data reduction and cell refinement were performed using the programs SMART and SAINT¹⁵. The absorption corrections were carried out empirically. The structure was solved by direct methods and refined by full-matrix least-squares against F^2 of data using the SHELXTL software package^{16,17}. The crystal data and experimental parameters relevant to the structure determination are listed in Table-1. Selected bond lengths and bond angles are listed in Table-2.

TABLE-1
CRYSTAL DATA AND STRUCTURE
REFINEMENT FOR $[Ni(AIDB)_2](pic)_2$

Molecular formula	$C_{50}H_{42}N_{16}O_{14}Ni$
Molecular weight	1149.71
Temperature (K)	293(2)
Crystal system	Monoclinic
Space group	C 2/c
Unit cell dimensions ($\text{\AA}, ^\circ$)	
a	23.40 (4)
b	19.39 (4)
c	17.50 (3)
α	90
β	121.68 (2)
γ	90
Volume (\AA^3), Z	6757 (21), 4
Calculated density ($g\ cm^{-3}$)	1.130
F(000)	2376
Crystal size (mm^3)	0.40 × 0.38 × 0.30
θ Range for data collection ($^\circ$)	1.47 - 25.50
Reflections collected	20059
Independent reflection	6111 [$R_{int} = 0.1080$]
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	6111/8/366
Goodness-of-fit on F^2	1.001
Final R indices [$I > 2\sigma(I)$]	$R1 = 0.1261, wR2 = 0.3025$
R indices (all data)	$R1 = 0.1671, wR2 = 0.3406$
Largest differences peak and hole ($e\ \text{\AA}^{-3}$)	1.431 and -0.730

TABLE-2
SELECTED BOND LENGTHS (\AA) AND BOND ANGLES ($^\circ$)

Bond length			
Ni(1)-N(3)#1	2.043(5)	Ni(1)-N(3)	2.043(5)
Ni(1)-N(5)#1	2.049(5)	Ni(1)-N(5)	2.049(5)
Ni(1)-N(1)	2.296(5)	Ni(1)-N(1)#1	2.296(5)
Bond angle			
N(3)#1-Ni(1)-N(3)	102.3(3)	N(3)#1-Ni(1)-N(5)#1	86.7(2)
N(3)-Ni(1)-N(5)#1	103.79(19)	N(3)#1-Ni(1)-N(5)	103.79(19)
N(3)-Ni(1)-N(5)	86.7(2)	N(5)#1-Ni(1)-N(5)	163.4(2)
N(3)#1-Ni(1)-N(1)	176.62(15)	N(3)-Ni(1)-N(1)	77.0(2)
N(5)#1-Ni(1)-N(1)	90.2(2)	N(5)-Ni(1)-N(1)	79.5(2)
N(3)#1-Ni(1)-N(1)#1	77.0(2)	N(3)-Ni(1)-N(1)#1	176.62(15)
N(5)#1-Ni(1)-N(1)#1	79.5(2)	N(5)-Ni(1)-N(1)#1	90.2(2)
N(1)-Ni(1)-N(1)#1	104.0(3)	-	-

CCDC 991078 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

RESULTS AND DISCUSSION

IR and UV spectra: For ligand AIDB, a strong band is found at $1558\ cm^{-1}$ together with a weak band at $1161\ cm^{-1}$. By analogy with previous assignments, the former can be attributed to $\nu_{(C=C)}$, while the latter can be attributed to benzimidazole rings^{18,19}. The bands are shifted by around $20\text{--}30\ cm^{-1}$ in the complex which implies direct coordination of the nitrogen to the metal ion. The results agree with those determined by X-ray diffraction. The UV bands of AIDB (277 nm) are marginally shifted (3 nm) in the complex, which is a clear evidence of C=N coordination to Ni(II). The absorption band is assigned to $\pi \rightarrow \pi^*$ (benzimidazole) transitions.

X-ray structure determination of complex: As shown in Fig. 1, the crystal structure of the complex consists of a discrete $[Ni(AIDB)_2]^{2+}$ cation and two picrate anions. The central Ni(II) is six-coordinate and the coordination sphere around Ni(II) is distorted octahedral. The ligand acts as a tetradentate N-donor. The maximum distance between Ni(II) and nitrogen atoms is $2.296\ (5)\ \text{\AA}$, the minimum distances is $2.043\ (5)\ \text{\AA}$, so N atoms are strongly coordinated. In the complex, adjacent two benzimidazole rings are concatenated by the $\pi \cdots \pi$ interactions ($d = 3.693\ \text{\AA}$), two adjacent picrate anions are inlaid in the coordination cation and concatenated by the $\pi \cdots \pi$ interactions ($d = 3.354\ \text{\AA}$).

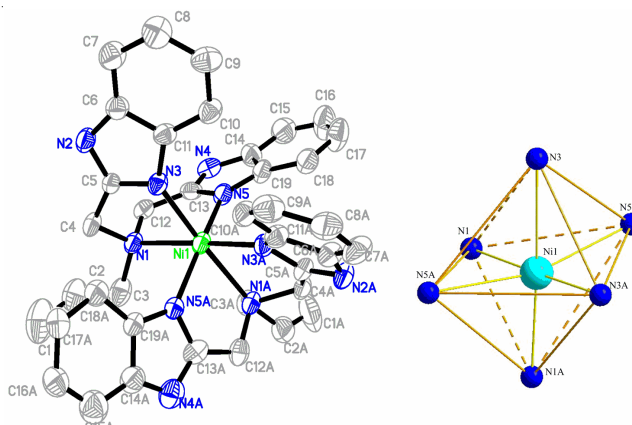


Fig. 1. Molecular structure and atom-numberings of $[Ni(AIDB)_2]^{2+}$ with hydrogen atoms omitted for clarity

Antioxidant activities

Hydroxyl radical scavenging activity: Hydroxyl radicals were generated in aqueous media through the Fenton-type reaction^{20,21}. The concrete method proceed following the procedure²². The absorbance was then measured at 520 nm. All the tests were run in triplicate and the results are expressed as the mean²³. The scavenging effect for OH^\bullet was calculated from the following expression:

$$\text{Scavenging ratio (\%)} = \frac{(A_i - A_0)}{(A_c - A_0)} \times 100$$

where A_i = absorbance in the presence of the test compound; A_0 = absorbance of the blank; A_c = absorbance in the absence

of the test compound, EDTA-Fe(II) and H_2O_2 . We compared the ability of the present compound to scavenge hydroxyl radicals with those of the well-known natural antioxidants mannitol and vitamin C, using the same method as reported²⁴. The 50 % inhibitory concentration (IC_{50}) value of mannitol and vitamin C are about 9.6×10^{-3} and 8.7×10^{-3} M, respectively. According to the antioxidant experiments, the IC_{50} values of the Ni(II) complex is 5.81×10^{-5} M (Fig. 2), which implies that the complex exhibits better scavenging activity than mannitol and vitamin C.

Superoxide radical scavenging activity: The concrete method proceed following the procedure²¹. The reactions were monitored at 560 nm with a UV/visible spectrophotometer and the rate of absorption change was determined. The percentage inhibition of NBT reduction was calculated using the following equation²⁵:

$$\text{NBT reduction (\%)} = \frac{1 - k'}{k} \times 100$$

where k' and k present the slopes of the straight line of absorbance values as a function of time in the presence and absence of SOD mimic compound (SOD is superoxide dismutase), respectively. The IC_{50} values for the complexes were determined by plotting the graph of percentage inhibition of NBT reduction against the increase in the concentration of the complex. The concentration of the complex which causes 50 % inhibition of NBT reduction is reported as IC_{50} . The Ni(II) complex shows an IC_{50} value of 6.77×10^{-5} M (Fig. 2), which indicates that it has potent scavenging activity for the superoxide radical ($\text{O}_2^{\cdot -}$). The Ni(II) complex exhibits good superoxide radical scavenging activity and may be an inhibitor (or a drug) to scavenge superoxide radicals ($\text{O}_2^{\cdot -}$) *in vivo* which needs further investigation.

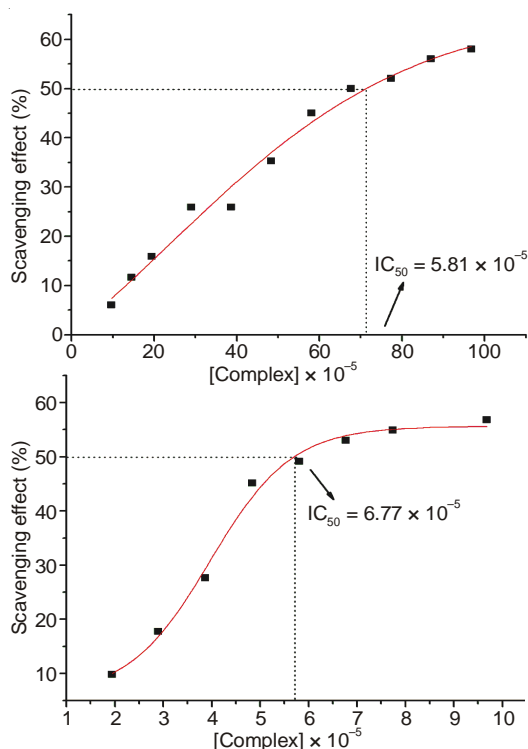


Fig. 2. Plots of hydroxyl radical scavenging effect (%) for the Ni(II) complex (above); plots of superoxide radical scavenging effect (%) for the Ni(II) complex (below)

Conclusion

In this paper, a new Ni(II) complex of *bis*(benzimidazol-2-ylmethyl)allylamine (AIDB) has been synthesized and characterized. The antioxidant properties of Ni(II) complex were investigated by hydroxyl radical scavenging activity and superoxide radical scavenging activity and the complex shows stronger scavenging effects. These results should prove useful in design of new antitumor drug and antioxidants.

ACKNOWLEDGEMENTS

The present research was supported by the Fundamental Research Funds for the Gansu Province Universities (212086), National Natural Science Foundation of Gansu Province (Grant No. 1212RJZA037) and 'Qing Lan' Talent Engineering Funds for Lanzhou Jiaotong University.

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