

二(2-羟基-4-甲氧基苯乙酮)镍(II)配合物的合成、 结构与抗微生物活性研究

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摘要: 合成了配合物二(2-羟基-4-甲氧基苯乙酮)镍(II), 并通过元素分析, 红外波谱以及 X-射线衍射单晶结构分析对标题化合物进行表征。晶体属 $P2_1/n$ 空间群。抑菌实验表明, 目标产物对沙门氏菌、金黄色葡萄球菌、短小芽孢杆菌以及大肠杆菌有一定的抑制作用。对该配合物的量子计算采用 hyperchem 程序包的半经验方法 ZINDO/1。计算了该配合物的最优化结构, 前沿轨道分布和主要原子电荷分布, 计算结果符合晶体结构的配位环境。

关键词: Ni(II)配合物; 丹皮酚; 晶体结构; 抗微生物活性

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Synthesis, Crystal Structure and Antimicrobial Study of a Complex Bis(2-hydroxy-4-methoxyacetophenone) Nickel(II)

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Abstract: A complex bis(2-hydroxy-4-methoxyacetophenone) Nickel(II) was synthesized and characterized by elemental analysis, IR and X-ray diffraction single-crystal structure analysis. The complex crystallizes in monoclinic system, space group $P2_1/n$ with $a=0.661\ 67(16)$ nm, $b=0.791\ 36(19)$ nm, $c=1.691\ 8(4)$ nm, $\beta=94.428(3)^\circ$, $V=0.883\ 2(4)$ nm³. Antimicrobial activity study found that the complex was active against *Salmonella species*, *Staphylococcus aureus*, *Bacillus pumilus* and *Escherichia coli*. Quantum chemistry calculation was performed to the complex by using semi-empirical method with ZINDO/1 of hyperchem 7.0 program package. The optimized structure have been investigated. Frontier molecular orbital components and atomic charge distributions had a good agreement for the coordinated condition in the crystal structure. CCDC: 643531.

Key words: nickel complex; paeonol; crystal structure; antimicrobial activity

Paeonol, 2-hydroxyl-4-methoxyacetophenone, is an effective component of many traditional Chinese medicines, and its ramifications have attracted considerable

attention because of their potential biological properties^[1,2]. Recently, A few new derivatives of paeonol have been prepared and characterized^[3-6], and our group have

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reported a series ramifications of paeonol also^[7-12]. However, to our knowledge, neither complete theoretical investigations nor comparison between the calculated and experimental results for these ramifications are available, which attracted our attention and prompted us to make a study. Therefore we synthesized the title complex and characterized it by IR spectra and X-ray diffraction single crystal structure analysis. On one hand, we applied semi-empirical to optimize the geometry; on the other hand, comparison between the calculated results and experimental values are performed.

In this study, we will report the preparation, crystal structure, toxicity study and quantum chemistry calculation of the complex, derived from paeonol and nickel acetate. We hope these investigations are helpful for providing insight into the structures and macroscopic properties of the derivatives of the title complex.

1 Experiment

1.1 Materials and instrumentation

All starting materials were of chemical purity. The solvents used in the physical measurements were of analytical purity. Elemental analyses were determined with a Perkin-Elmer 240c instrument. Solution electrical conductivity was measured by a BSD-A numerical conductometer (Jiangsu, China) with solution concentration of $1.0 \times 10^{-3} \text{ mol} \cdot \text{dm}^{-3}$ in methanol at 297 K. IR spectrum was measured as KBr discs using a Nicolet 5DX FTIR spectrophotometer. UV-vis spectrophotometer have been determined on the Dao jing UV-2250, the solvent is methanol, quartz groove, area: 0~5.0ABS, wavelength: 800~200 nm, scanning speed: 300 nm·min⁻¹, response: 0.05.

1.2 Preparation of title compound

[NiPae₂]: To a stirred solution of Ni (AC)₂·4H₂O (0.248 g, 1 mmol) in 30 mL absolute methanol was added dropwise a solution of paeonol (0.332 g, 2 mmol) in 10 mL absolute methanol at room temperature. The mixture was stirred and refluxed for 2 hours at 55 °C, and then cooled to room temperature. Violet microcrystal were precipitated and filtered off, washed with methanol and dried in vacuo, yield 41%. m.p. 294.0 °C (dec.). Anal. calc. for C₁₈H₁₈NiO₆ (%): C,

55.49; H, 4.62; Found (%): C, 55.52; H, 4.63.

The supernatant fluid was filtered again and 30 mL solution was placed in an ambient environment. After two weeks, a violet single crystal suitable for X-ray structure determination was obtained by slow evaporation.

CCDC: 643531.

1.3 Crystallographic data collection and structure determination

A violet single crystal of dimensions 0.18 mm × 0.10 mm × 0.08 mm was selected for structure determination. The crystal data were collected at 298(2) K on a Siemens Smart/CCD area-detector diffractometer with Mo K α radiation ($\lambda=0.071\ 073\ \text{nm}$) over the range $2.41^\circ \leq \theta \leq 25.01^\circ$ with an ω - 2θ scan mode. A absorption correction was made using SADABS software. The structure was solved using the direct methods with the program SHELXS-97^[13], refined using full-matrix least-squares on F^2 with anisotropic thermal parameters for all nonhydrogen atoms with the program SHELXL-97^[14]. The hydrogen atoms were added according to theoretical models. The final refinement converged at $R=0.037\ 8$ and $wR=0.101\ 3$ for 1 247 observed reflections with $I>2\sigma(I)$ ($W=1/[\sigma^2(F_o^2) + (0.057\ 0P)^2 + 0.612\ 4P]$ where $P=(F_o^2+2F_c^2)/3$), $S=1.046$ and $(\Delta/\sigma)_{\text{max}}=0.000$. The largest peak and deepest hole on the final difference Fourier map are 409 and $-366\ \text{e} \cdot \text{nm}^{-3}$, respectively.

1.4 Computational methods

The initial molecular geometry were optimized by using MM+ molecular modeling. Subsequently, the semi-empirical method with ZINDO/1 was performed with hyperchem professional 7.0 software package. All calculations were performed on a Pentium IV computer using the default convergence criteria.

1.5 Antimicrobial activity

As a preliminary screening for antimicrobial activity, the title complex was tested against standard strains of Salmonella species CMCC (B) 50 094, Staphylococcus aureus CMCC (B) 26 003, Bacillus pumilus CMCC (B) 63 202 and Escherichia coli CMCC (B) 44 102, using the modified agar diffusion method as described in the literature^[15]. For the comparison, the antimicrobial activity of Ni(AC)₂·4H₂O and paeonol

were also tested. The compounds were dissolved in DMF. Nutrient agar thawed by heating in water bath was transferred to plates and froze at 37 °C. After test strains were spread on the solid nutrient agar surface, stainless steel tubes (7.8 × 6 × 10 mm) were placed vertically on the surface. 0.04 mL compound with certain concentration were injected to the steel tubes. They were allowed to incubate at 37 °C for 24 hour. The inhibition zone around the disc was calculated as zone diameter in millimeters. Blank tests showed that DMF in the preparation of the test solutions does not affect the test organisms. All tests were repeated three times and average data were taken as the final result.

2 Results and discussion

2.1 Spectral characteristics

The structure of the title complexes were further confirmed by spectral characteristics. The IR and UV spectra of the title complex are shown in Fig.1 and Fig.2.

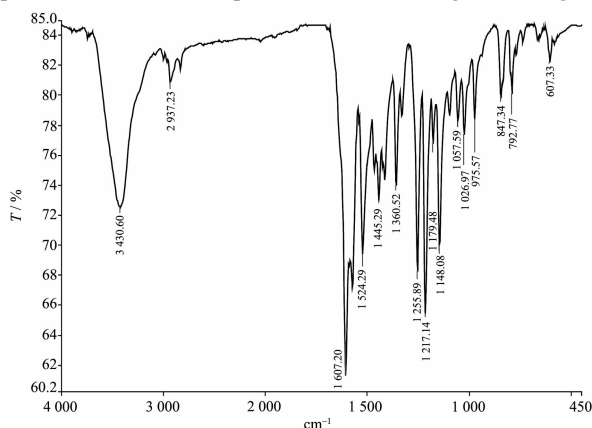


Fig.1 IR spectrum of the title complex

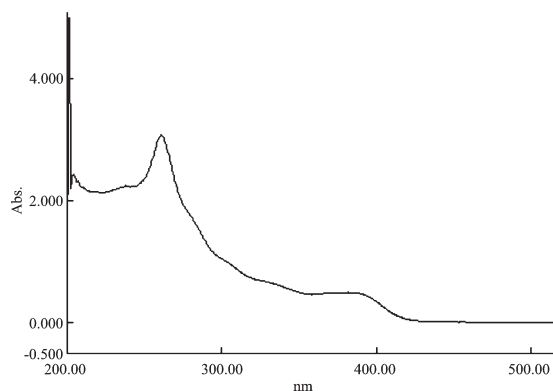


Fig.2 UV-Vis spectrum of the title complex

As Fig.1 shows a middle peak at 2 937 cm^{-1} is characteristic of stretching vibration of the phenyl

group C-H bonds of paeonol. In range of 1 524~1 340 cm^{-1} , the bonds are characteristic of skeleton vibration of phenyl ring.

The strong stretching bands appeared at 1 607 cm^{-1} indicating carbonyl groups of paeonol. The stretching bands O-H appeared at 3 430 cm^{-1} indicating solvent methanol. The strong $\nu(\text{O-H})$ band originally found in the ligand paeonol disappeared on complexation indicating deprotonation of the phenolic hydroxyl group and coordination of phenolic oxygen to the metal ion. This is in agreement with molar conductivity of the complex ($\Lambda_{\text{M}}(\text{CH}_3\text{OH}, 289 \text{ K})=38 \text{ S} \cdot \text{cm}^2 \cdot \text{mol}^{-1}$), which is attributable to non-electrolyte and molecular complex.

The UV-Vis electronic absorption spectra of the title compound has been obtained. The spectrum of the title compound exhibits two bands at 260 nm and 382 nm. The band of 260 nm belongs to the $\pi-\pi^*$ transition of the ligand paeonol, and the peak at 382 nm is ascribed to the paeonol ligand to metal charge transfer.

2.2 Crystal structure and optimized geometry

Some selected X-ray diffraction data together with the optimized geometrical parameters at semi-empirical ZINDO/1 are listed in Table 1.

Comparing the optimized geometry with the experimental data in Table 1, it can be found that most of the optimized bond lengths are slightly short to the experimental values and bond angles are slightly similar to the experimental values. The average deviation of predicted bond lengths, Ni-O bond lengths, with semi-empirical method to experimental value is 0.000 145 nm. Therefore, the predicted bond lengths with semi-empirical method correlates well for the experimental value. The average difference between experimental and calculated semi-empirical bond angles is 1.61°. Thereby, on the whole, the optimized bond lengths and bond angles obtained by semi-empirical method show better agreement with the experimental values and the most important structure feature of the title complex does not change.

The atomic numbering scheme of the title compound is displayed in Fig.3. The title compound, $[\text{Ni}(\text{C}_9\text{H}_9\text{O}_3)_2]$, has its metal atom in a square-planar

Table 1 Some selected bond lengths (nm) and bond angles (°) of the title compound

Bond lengths	Experiment	ZINDO	Bond lengths	Experiment	ZINDO
Ni(1)-O(1)	0.184 6(2)	0.186 3	Ni(1)-O(2)	0.182 3(2)	0.181 1
Ni(1)-O(2)#1	0.182 3(2)	0.181 0	Ni(1)-O(1)#1	0.184 6(2)	0.186 2
O(1)-C(2)	0.130 1(4)	0.130 8	O(2)-C(4)	0.131 2(3)	0.133 8
O(3)-C(6)	0.136 5(3)	0.137 0	O(3)-C(9)	0.142 3(4)	0.138 5
Bond angles	Experiment	ZINDO	Bond angles	Experiment	ZINDO
O(2)#1-Ni(1)-O(2)	180.00(15)	176.870	O(2)#1-Ni(1)-O(1)	86.32(10)	85.519
O(2)-Ni(1)-O(1)	93.68(10)	94.565	C(2)-O(1)-Ni(1)	130.7(2)	128.731
C(4)-O(2)-Ni(1)	127.8(2)	128.681	C(6)-O(3)-C(9)	117.8(2)	115.256

#1: $-x+2, -y, -z$.

trans-NiO₄ coordination environment; the Ni (II) atom lies on a center of symmetry. Ni (II) atom is four-coordinated with the coordination surrounding of closely square-planar by the four O atoms of paeonol. In a molecule unit, hydrogen atom of hydroxyl of paeonol were lost during the formation of coordinate bond for the charge balance.

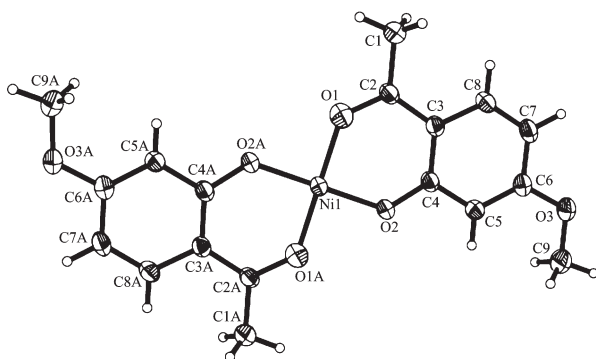


Table 2 Non-H atoms charges and contributive percents of frontier orbital of the title complex

Atoms	Charges	Frontier orbital /%		Atoms	Charges	Frontier orbital /%	
		HOMO	LUMO			HOMO	LUMO
Ni(1)	0.186 837	9.341 9	6.915 8	C(1A)	-0.226 462	0.147 283	4.108 983
C(1)	-0.226 518	0.216 834	6.577 584	C(2A)	0.386 144	0.490 203	0.839 417
C(2)	0.386 156	0.489 107	0.821 355	C(3A)	-0.182 078	1.752 746	3.273 106
C(3)	-0.182 088	1.751 136	3.194 523	C(4A)	0.334 299	3.808 212	1.674 727
C(4)	0.334 292	3.808 713	1.641 268	C(5A)	-0.237 835	19.314 91	2.696 088
C(5)	-0.237 85	19.309 7	2.655 176	C(6A)	0.287 363	0.697 594	0.075 602
C(6)	0.287 354	9.134 808	0.492 019	C(7A)	-0.160 737	0.888 903	7.039 373
C(7)	-0.160 763	0.889 241	6.890 594	C(8A)	0.044 266	8.722 81	0.482 13
C(8)	0.044 278	8.712 728	0.469 547	C(9A)	0.040 731	4.649 54	5.482 548
C(9)	0.040 677	4.644 39	5.358 25	O(1A)	-0.369 279	0.342 994	16.95 982
O(1)	-0.369 27	0.342 886	16.608 87	O(2A)	-0.302 156	0.049 687	0.373 198
O(2)	-0.302 116	0.049 423	0.002 782	O(3A)	-0.257 626	0.033 492	0.036 817
O(3)	-0.257 605	0.033 469	0.035 04				

2.4 Antimicrobial activity

From the data of Table 3, it is observed that the title complex, paeonol and $\text{Ni}(\text{AC})_2 \cdot 4\text{H}_2\text{O}$ exhibited antibacterial activity against all test bacterial organisms. In the test range, these compounds were more active against the strains with the increase of concentration. The highest antimicrobial activity of paeonol ligand was observed against *Escherichia coli*

and almost no difference in toxicity against *Bacillus pumilus* between $\text{Ni}(\text{AC})_2 \cdot 4\text{H}_2\text{O}$ and the title complex $[\text{NiPae}_2]$. The ligand paeonol show higher activity against all test bacterial organisms as compared to the title complex. The reason may be attributed to the properties of paeonol, which has been reported to possess analgesic, sedative, antiallergic, antioxidative, antiinflammatory and antimicrobial properties.

Table 3 Diameter of inhibition zone

Compound	Concentration / (mmol · L ⁻¹)	Diameter of inhibition zone / mm			
		<i>Salmonella species</i>	<i>Escherichia coli</i>	<i>Bacillus pumilus</i>	<i>Staphylococcus aureus</i>
$\text{Ni}(\text{AC})_2 \cdot 4\text{H}_2\text{O}$	5.0	14.9	15.0	13.0	10.6
	2.5	13.6	14.9	12.2	9.5
	1.2	13.0	12.6	11.9	9.2
	0.6	12.8	12.2	9.2	9.0
[NiPae ₂]	5.0	13.3	14.2	13.1	13.0
	2.5	12.0	13.8	12.2	12.8
	1.2	11.1	13.1	11.5	12.5
	0.6	10.2	11.2	10.0	12.4
Paeonol	5.0	13.4	15.9	14.6	13.8
	2.5	12.1	14.8	13.5	13.2
	1.2	10.6	13.8	12.7	12.9
	0.6	10.1	12.1	9.9	10.2

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