Standard molar enthalpy of formation of \([(\text{C}_{12}\text{H}_{8}\text{N}_{2})_{2}\text{Bi}(\text{O}_{2}\text{NO})_{3}\)]\) and its biological activity on \(\text{Schizosaccharomyces pombe}\)

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Abstract The title complex \([(\text{C}_{12}\text{H}_{8}\text{N}_{2})_{2}\text{Bi}(\text{O}_{2}\text{NO})_{3}\)]\) was synthesized by reaction of 1,10-phenanthroline (phen) and Bi(NO\(_3\))\(_3\)·5H\(_2\)O. The structure of the complex was characterized by single-crystal X-ray diffraction, IR spectroscopy, and elemental analysis. An advanced solution-reaction isoperibol microcalorimeter was applied to determine the standard molar enthalpies of formation at 298.15 K of the complex and Bi(NO\(_3\))\(_3\)·5H\(_2\)O, giving \(-\langle 798.92 \pm 5.99 \rangle\) and \(-\langle 1986.87 \pm 0.20 \rangle\) kJ mol\(^{-1}\), respectively. The biological effect of the complex was evaluated by microcalorimetry on the growth of \(\text{Schizosaccharomyces pombe}\) (\(\text{S. pombe}\)). According to thermogenic curves, the corresponding thermokinetics and thermodynamic parameters were derived. The complex had good bioactivity on the growth metabolism of \(\text{S. pombe}\), with the value of IC\(_{50}\) being \(2.8 \times 10^{-5}\) mol L\(^{-1}\).

Keywords 1,10-Phenanthroline · Bismuth(III) complex · Standard molar enthalpy of formation · Thermodynamic parameters · Microcalorimetry

Introduction

In recent years, much attention has been paid to the design and construction of bismuth compounds because of their high effectiveness and low toxicity in the treatment of microbial infections, such as syphilis, diarrhea, gastritis, and colitis. In particular, radioisotope \(^{212}\text{Bi}\) and \(^{213}\text{Bi}\) compounds exhibited good anticancer activities and could reduce the side-effects of cisplatin (cis-DDP) in carcinoma treatment [1, 2]. Bismuth is considered nowadays as a relatively non-toxic heavy metal. The bismuth(III) atom, possessing a larger ionic radius (1.16 Å) and one inert electron pair (6\(^{s}\)\(^2\)), can form complexes with higher coordination numbers (from 3 to 10), resulting in producing some irregular structure of bismuth(III) compounds [3, 4]. The affinity of bismuth(III) for nitrogen donors has been reported for a range of ligands including glycine and a number of bidentate nitrogen donors. Among these nitrogen-base ligands, 1,10-phenanthroline has gained more prominence in the coordination chemistry, mainly to have unusual structural features, such as its rigidity, planarity and hydrophobicity [5–7]. The two nitrogen atoms are permanently placed in juxtaposition, ideal for bidentate binding to metal ions. Owning to its planarity, phen derivatives and their metal complexes are able to intercalate with DNA and RNA via aromatic \(\pi\)-stacking [8]. More importantly, some metal complexes can efficiently cleave the DNA backbone, especially for the complex \([\text{Cu(phen)}_{2}]^{2+}\) used in molecular biology as DNA cleaving reagent [9].

Biological microcalorimetry, providing a continuous measurement of heat production, is very suitable for the survey of heat-output of slightly exothermic or endothermic processes, such as the heat production of microbial cells, organelles, tissues and organs [10–12]. It can provide a general analytical tool for characterization of cell growth process and has been extensively used to investigate the interaction between drug and cultured cell [13]. In this study, as a part of our continuing studies [14–16], we have prepared a ten-coordinate 1:2 adduct \([(\text{C}_{12}\text{H}_{8}\text{N}_{2})_{2}\text{Bi}(\text{O}_{2}\text{NO})_{3}\)]\).

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by reacting of Bi(NO$_3$)$_3$·5H$_2$O and the aromatic bidentate
base 1,10-phenanthroline. The crystal structure of the com-
plex has been reported by Barbour et al. [17]. However, up to
now, the enthalpies of formation of the complex, together
with bismuth nitrate pentahydrate, have not been accurately
determined [18]. As we all know, the thermochemical
parameters are an indispensable part of chemical thermo-
dynamics, which closely relates to fundamental academic
problems together with application development. Therefore,
on the basis of previous work [19], the thermochemical
properties of the complex were planned to be investigated.
Then *S. pombe* was used as an ideal model to evaluate the
biological activity of the complex by microcalorimetry. This
is because that the constitution of human cells are very
complicated, which make them difficult to study. In com-
parison, *S. pombe*, also called “fission yeast,” which has a
distinct mitotic cycle, have many similar facts with human
cells and are relatively ease to be operated by cytology
technique [20]. Many scientific findings in human cells are
first investigated in yeast cells [21]. In the experiments, we
found that, like the previously reported bismuth(III) complex
[15], the current complex also showed good inhibitory
activity toward *S. pombe* growth. To fully study the bio-
logical effect of the complex, some thermodynamics and kinetic
data were derived according to the power–time curves
obtained from the microcalorimeter. The relationship
between the concentration of the complex and the growth of
*S. pombe* was analyzed by the thermokinetics model.

**Experimental**

**Chemicals and instruments**

All chemicals were purchased from commercial sources
and used as received; no further purification was done. The
triply distilled water was used in all the studies. *S.pombe*
(ACCC 20047) was provided Agricultural Culture Col-
lection of China. The Edinburgh minimal medium (EMM)
culture composition was K$_2$HPO$_4$ 3 g, Na$_2$HPO$_4$ 2.2 g,
NH$_4$Cl 5 g, and Glucose 20 g. The yeast extract medium
composition was 20 mL and H$_2$O 1000 mL (natural pH).

FTIR spectra were determined in the range of
4000–400 cm$^{-1}$ on an Avatar 360 (Nicolet, Madison,
USA) spectrophotometer using a KBr pellet with a reso-
lation of 2 cm$^{-1}$. Absorption spectra were taken with a
Hitachi U-3010 UV/Vis spectrophotometer with 1-cm
quartz, in the range 190–1,100 nm at 298.15 K. The
refractive indexes were done with a S2WA-Z digital Abbe
refractometer. Thermochemical analysis was measured
using a SCR-100 solution-reaction isoperibol calorimeter,
which was constructed by the Thermochemical Laboratory
of Wuhan University, China [22]. The microcalorimetric
study was performed on a 3116-2/3239 TAM Air
calorimeter (Thermometric AB, Sweden) [16]. An ele-
mental analyzer (PerkinElmer 2400 II) was used to mea-
sure the C, H, and N contents of the complex. Single-
crystal X-ray diffraction data for the complex were col-
lected on a Bruker SMART CCD diffractometer at
153(2) K using graphite monochromated Mo-Kα radiation
(λ = 0.71073 Å) and were used to measure cell dimen-
sions and diffraction intensities. The structure was solved
by the direct methods and refined by full-matrix least
squares on $F^2$ using the SHELXTL-97 program.

**Synthesis of Bi(NO$_3$)$_3$·5H$_2$O**

Bi$_2$O$_3$ (2 × 10$^{-3}$ mol, 0.9319 g) was dissolved in HNO$_3$
(8 mol L$^{-1}$, 5 mL). After continuously stirred for 3 h, the
reaction mixture was filtered, and some colorless crystals
were obtained by slow evaporation of the filtrate. The water
content of the synthetic sample was determined by differ-
ence and thermogravimetric/differential thermogravimetric
(TG–DTG) curves. The TG and DTG curves of the sample,
were shown in Fig. 1. When the degradation temperature varies
from 342.05 to 385.55 K, the mass loss is 18.49%, which
roughly coincides with the value of 18.55%, calculated for
the loss of 5 mol of H$_2$O from Bi(NO$_3$)$_3$·5H$_2$O. These facts
have shown that Bi$_2$O$_3$ can react with HNO$_3$ (8 mol L$^{-1}$)
and provide with Bi(NO$_3$)$_3$·5H$_2$O.

**Preparation of the complex [(C$_{12}$H$_8$N$_2$)$_2$Bi(O$_2$NO)$_3$]**

In a typical experimental procedure, Bi(NO$_3$)$_3$·5H$_2$O
(4 × 10$^{-4}$ mol, 0.194 g) and mannitol (4 × 10$^{-4}$ mol,
0.0728 g) were ground into a smooth paste in an appro-
priate mortar [15]. To this was added 3 mL deionized water
and 5 mL methanol in turn and stirred until dissolution.
Subsequently, the mixed solution was slowly added

![Fig. 1 TG–DTG curves of Bi(NO$_3$)$_3$·5H$_2$O](image)
The enthalpy of dilution of nitric acid (8 mol L⁻¹, 1HNO₃ + 5.119 H₂O)

The prepared nitric acid (8 mol L⁻¹, 1HNO₃ + 5.119 H₂O) was obtained by diluting 16 mol L⁻¹ nitric acid (w = 69.2%, ρ = 1.42 g mL⁻¹) with water. The prepared nitric acid (8 mol L⁻¹) is regarded as 1HNO₃ in 5.119 H₂O. According to the reported literature [18], plot of dilution enthalpy against the molar amount of water is shown Fig. 2. Using the Expdec1 curve fitting from data of the dilution enthalpy (ΔdHₘ) with the molar amount of water n(H₂O), the curve equation was obtained:

\[
\Delta dH^\circ_m = -205.948 + 28.486 \exp(nH_2O/2.232) \\
= -205.948 + 28.486 \exp(-5.119/2.232) \\
= -205.948 + 28.486 \times 0.10095 \\
= -205.948 + 2.786 \\
= -203.07 \text{kJ mol}^{-1}
\]

The enthalpy of dilution of (1HNO₃ + 5.119 H₂O) was calculated to be ΔdHₘ [5.119:1 HNO₃(aq), 298.15 K] = −203.07 kJ mol⁻¹.

Thermochemical cycle

The complex was synthesized by the following reaction:

\[
\text{Bi(NO}_3\text{)}_3 \cdot 5\text{H}_2\text{O(s)} + 2\text{C}_1\text{H}_8\text{N}_2 \cdot \text{H}_2\text{O(s)} \rightarrow \text{[(C}_1\text{H}_8\text{N}_2)\text{)_2Bi(O}_2\text{NO}_3]\text{(s) + 7H}_2\text{O(l) (1)}
\]

Based on Hess’s law, a thermochemical cycle was designed (as shown in Fig. 3). An ideal mixed calorimetric solvent S (V_DMSO/V_HNO₃ (w_HNO₃:20%) = 8:3) was prepared through testing for many times, which had a good solubility for all of the relevant samples on the premise of thermochemical cycle. The standard molar dissolution enthalpies of the samples were determined successively by a solution-reaction calorimeter, and the obtained results were applied to calculate the standard molar enthalpy of the reaction, so as to further estimate the standard molar enthalpy of formation of the complex.

To further confirm the feasibility of the thermochemical cycle, the UV spectra and refractive indexes of solution B and D were determined, respectively. The experimental results showed that solution B and D had similar UV spectrum curves (Fig. 4) and equal refractive indexes (n_25 = 1.4130). These facts indicated that solution B and D had the same thermodynamic state, which demonstrated that the thermochemical cycle was reasonable.

Determination of dissolution enthalpies of the samples

The structure of the solution-reaction isoperibol calorimeter (SRC-100) has been elucidated in the reported literature [22]. A Dewar vessel, possessing a 100 mL internal volume and a twin-blade stirrer, was immersed in the water thermostat. In the calorimetric experiments, the precision values of temperature control and temperature measurement were ± 0.001 and ± 0.0001 K, respectively. The temperature, the current, and the resistance of the heater were 298.15 K, 21.813 mA, and 1212.3 Ω, respectively. Before use, the calibration of the calorimeter was performed by measuring the dissolution enthalpies of tris(hydroxymethyl)aminomethane (THAM; NBS 742a, USA) in 0.0001 mol L⁻¹ HCl and KCl (calorimetric primary standard) in triply distilled water at 298.15 K. In our experiments, after five parallel measurements, the mean dissolution enthalpies were (17,588 ± 13) J mol⁻¹ for KCl and [−(29,751 ± 14)] J mol⁻¹ for THAM, in agreement with published data, (17,536 ± 9) J mol⁻¹ for the primary standard.
KCl [22] and [(29,766 ± 31.5)] J mol⁻¹ for THAM [23]. The dating error was within ± 0.5%, which indicated that the calorimeter was reliable.

The content of the prepared complex was determined by EDTA titration method, which suggested its purity was greater than 99.0%. All of the solid samples were dried and ground fully in advance. The volume of calorimetric solvent was 100 mL for each time. When the calorimeter was adjusted to a constant temperature of (298.150 ± 0.001) K, the samples were added into the reaction vessel, and their dissolution enthalpies were determined. The amount and measurement sequence of the relevant substances of reaction (1) are as follows:

1 mmol C₁₂H₈N₂H₂O(s) + S → Solution A
0.5 mmol Bi(NO₃)₃·5H₂O(s) + Solution A → Solution B
0.5 mmol [(C₁₂H₈N₂)₂Bi(O₂NO)₃(s)] + S → Solution C
3.5 mmol H₂O(l) + Solution C → Solution D

Five parallel experiments were carried out in each sample, and the obtained results are shown in Tables 1 and 2.

Microcalorimetric measurements

The microcalorimetry was carried out on a TAM air isothermal microcalorimeter at 32.00 °C. Baselines were taken before each measurement and the calorimeters were calibrated electrically. When the system has gained the stable baseline, 5 mL EMM sterilized culture medium was added into the sterilized sample ampoules. S. pombe was inoculated with an initial density of 1 × 10⁶ cells per mL. The sample at different concentrations was added to the cell suspension, respectively. Power–time curves for all measurements were performed at 32.00 °C. All of the microcalorimetric experiments were repeated three times, and the obtained results were identical.

Results and discussion

Crystal structure of the complex

X-ray crystallographic analysis indicated that the complex crystallized in a monoclinic space group of C2/c symmetry and its structure along with the atomic numbering scheme was shown in Fig. 5. Each unit of [(C₁₂H₈N₂)₂Bi(O₂NO)₃] consisted of one Bi³⁺ ion, two 1,10-phenanthroline ligands and three nitrate ions. The central bismuth atom was 10-coordinate being bound to three bidentate nitrate ions and four nitrogen atoms from two chelating phen units [17].
Standard molar enthalpy of formation of \([\text{[C}_{12}\text{H}_8\text{N}_2\text{]}_2\text{Bi(O}_2\text{NO})_3\text{]}\) and its biological activity…

Table 1  Determination of the reaction enthalpy of \([\text{Bi(NO}_3\text{)}_3\cdot\text{5H}_2\text{O(s)}]\) in 8 mol L\(^{-1}\) HNO\(_3\) (100 mL) at 298.15 K

<table>
<thead>
<tr>
<th>Reaction</th>
<th>No.</th>
<th>(m^a)g</th>
<th>(t^b)s</th>
<th>(\Delta H_m^c)/kJ mol(^{-1})</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bi(_2)O(_3) + (6HNO(_3) + 30H(_2)O) (\rightarrow) 2Bi(NO(_3))(_3) · 5H(_2)O + 23H(_2)O</td>
<td>1</td>
<td>0.23292</td>
<td>121.43</td>
<td>–151.235</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>0.23299</td>
<td>120.87</td>
<td>–151.819</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>0.23304</td>
<td>120.45</td>
<td>–151.101</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>0.23302</td>
<td>120.40</td>
<td>–151.467</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>0.23298</td>
<td>120.56</td>
<td>–151.300</td>
</tr>
</tbody>
</table>

\(\Delta H_m^c\) [Bi(NO\(_3\))\(_3\)·5H\(_2\)O (s), 298.15 K] = –(151.38 ± 0.28) kJ mol\(^{-1}\)

\(a\)  \(m\) mass of Bi\(_2\)O\(_3\)

\(b\)  \(t\) heating period of electrical calibration

\(c\) Uncertainty was estimated as twice the standard deviation of the mean of the results

Table 2  Dissolution enthalpies of \([\text{C}_{12}\text{H}_8\text{N}_2\cdot\text{H}_2\text{O(s)}]\), \([\text{Bi(NO}_3\text{)}_3\cdot\text{5H}_2\text{O(s)}]\), \([\text{C}_{12}\text{H}_8\text{N}_2\text{]}_2\text{Bi(O}_2\text{NO})_3\text{]}\), and \([\text{H}_2\text{O(l)}]\) in the calorimetric solvent S or corresponding solution (100 mL) at 298.15 K

<table>
<thead>
<tr>
<th>System</th>
<th>No.</th>
<th>(m^a)g</th>
<th>(t^b)s</th>
<th>(\Delta H_m^c)/kJ mol(^{-1})</th>
</tr>
</thead>
<tbody>
<tr>
<td>([\text{C}_{12}\text{H}_8\text{N}_2\cdot\text{H}_2\text{O(s)}]) in S</td>
<td>1</td>
<td>0.19823</td>
<td>14.375</td>
<td>–15.164</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>0.19797</td>
<td>14.328</td>
<td>–15.123</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>0.19804</td>
<td>14.483</td>
<td>–15.148</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>0.19806</td>
<td>14.512</td>
<td>–15.472</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>0.19810</td>
<td>14.390</td>
<td>–15.317</td>
</tr>
<tr>
<td>([\text{Bi(NO}_3\text{)}_3\cdot\text{5H}_2\text{O(s)}]) in the solution A</td>
<td>1</td>
<td>0.24274</td>
<td>18.812</td>
<td>20.061</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>0.24251</td>
<td>18.594</td>
<td>20.286</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>0.24264</td>
<td>18.453</td>
<td>20.781</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>0.24245</td>
<td>18.688</td>
<td>20.289</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>0.24245</td>
<td>18.813</td>
<td>20.267</td>
</tr>
<tr>
<td>([\text{C}_{12}\text{H}_8\text{N}_2\text{]}_2\text{Bi(O}_2\text{NO})_3\text{]}) in S</td>
<td>1</td>
<td>0.28736</td>
<td>21.631</td>
<td>22.782</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>0.28748</td>
<td>21.652</td>
<td>22.277</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>0.28795</td>
<td>21.631</td>
<td>22.241</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>0.28756</td>
<td>21.608</td>
<td>22.632</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>0.28774</td>
<td>21.659</td>
<td>22.856</td>
</tr>
<tr>
<td>([\text{H}_2\text{O(l)}]) in the solution C</td>
<td>1</td>
<td>0.03786</td>
<td>2.390</td>
<td>–0.39180</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>0.03790</td>
<td>2.450</td>
<td>–0.35988</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>0.03784</td>
<td>2.421</td>
<td>–0.34485</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>0.03782</td>
<td>2.468</td>
<td>–0.37795</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>0.03789</td>
<td>2.141</td>
<td>–0.33502</td>
</tr>
</tbody>
</table>

\(\Delta H_m^c\) [H\(_2\)O(l), 298.15 K] = –(0.36 ± 0.02) kJ mol\(^{-1}\)

\(a\)  \(m\) mass of sample

\(b\)  \(t\) heating period of electrical calibration

\(c\) Uncertainty was estimated as twice the standard deviation of the mean of the results

Thermochemistry

Standard molar enthalpy of Bi(NO\(_3\))\(_3\)·5H\(_2\)O

The reaction enthalpy of Bi(NO\(_3\))\(_3\)·5H\(_2\)O was determined according to the following reaction:

\[
\text{Bi}_2\text{O}_3 + (6\text{HNO}_3 + 30\text{H}_2\text{O}) \rightarrow 2\text{Bi(NO}_3\text{)}_3 \cdot 5\text{H}_2\text{O} + 23\text{H}_2\text{O}
\]

As is shown in Table 1, the reaction enthalpy of Bi(NO\(_3\))\(_3\)·5H\(_2\)O was estimated to be \(\Delta H_m^c\) [Bi(NO\(_3\))\(_3\)·5H\(_2\)O(s), 298.15 K] = –(151.38 ± 0.28) kJ mol\(^{-1}\).
Fig. 5 SHELXTL diagram of the complex, showing the atom labeling scheme and 30% probability displacement ellipsoids. All hydrogen atoms are represented as small spheres of arbitrary radii.

\[ \Delta_r H_m^0[{\text{Bi(NO}_3)_3 \cdot 5\text{H}_2\text{O(s)}}], 298.15 \text{ K}] \]
\[ = 2\Delta_t H_m^0[{\text{Bi(NO}_3)_3 \cdot 5\text{H}_2\text{O(s)}}], 298.15 \text{ K}] + 23\Delta_t H_m^0[{\text{H}_2\text{O(l)}}], 298.15 \text{ K} \]
\[ - \Delta_t H_m^0[{\text{Bi}_2\text{O}_3(s)}], 298.15 \text{ K}] - 6\Delta_t H_m^0[{\text{HNO}_3(l)}], 298.15 \text{ K} \]
\[ - 30\Delta_t H_m^0[{\text{H}_2\text{O(l)}}], 298.15 \text{ K}] - \Delta_d H_m^0[5.119 : 1 \text{HNO}_3(aq)], 298.15 \text{ K}] \]

According to Ref. [18]

\[ \Delta_r H_m^0[{\text{H}_2\text{O(l)}}], 298.15 \text{ K}] = -(285.83 \pm 0.04) \text{ kJ mol}^{-1} \]
\[ \Delta_r H_m^0[{\text{Bi}_2\text{O}_3(s)}], 298.15 \text{ K}] = -573.88 \text{ kJ mol}^{-1} \]
\[ \Delta_r H_m^0[5.119 : 1 \text{HNO}_3(aq)], 298.15 \text{ K}] = -203.07 \text{ kJ mol}^{-1} \]
\[ \Delta_r H_m^0[{\text{HNO}_3(l)}], 298.15 \text{ K}] = -174.10 \text{ kJ mol}^{-1} \]

**Standard molar enthalpy of reaction (1)**

Based on Hess’ law and the dissolution enthalpies of the tested samples, the standard molar enthalpy of the reaction was obtained as follows:

\[ \Delta_r H_m^0(1a) = 2\Delta_t H_m^0(2a) + \Delta_t H_m^0(3a) - \Delta_t H_m^0(4a) - 7\Delta_t H_m^0(5a) \]
\[ = [2 \times (-15.24) + 20.34 - 22.56 - 7 \times (-0.36)] \]
\[ \pm \sqrt{[2 \times (0.27)^2 + (0.28)^2 + (7 \times 0.02)^2]} \]
\[ = -(30.18 \pm 0.51) \text{ kJ mol}^{-1} \]

(4)

**Standard molar enthalpy of formation of the complex**

According to Hess’ law and the principles of thermodynamics:

\[ \Delta_r H_m^0(1a) = \Delta_r H_m^0[(\text{C}_{12}\text{H}_8\text{N}_2)_2\text{Bi(O}_2\text{NO}_3)_3(s)], 298.15 \text{ K}] + 7\Delta_r H_m^0[\text{H}_2\text{O(l)}, 298.15 \text{ K}] - 2\Delta_r H_m^0[\text{C}_{12}\text{H}_8\text{N}_2 \cdot \text{H}_2\text{O(s)}, 298.15 \text{ K}] - \Delta_r H_m^0[\text{Bi(NO}_3)_3 \cdot 5\text{H}_2\text{O(s)}, 298.15 \text{ K}] \]

(5)

According to refs [18, 19, 24]
\[ \Delta H_m^0 [H_2O(l), 298.15 K] = -(285.83 \pm 0.04) \text{ kJ mol}^{-1} \]
\[ \Delta H_m^0 [C_{12}H_8N_2 \cdot H_2O(s), 298.15 K] = -(391.34 \pm 2.98) \text{ kJ mol}^{-1} \]
\[ \Delta H_m^0 [\text{Bi(NO}_3)_3 \cdot 5H_2O(s), 298.15 K] = -(1986.87 \pm 0.20) \text{ kJ mol}^{-1} \]
\[ \Delta H_m^0 [(C_{12}H_8N_2)_2\text{Bi(O}_2\text{NO)}_3(s), 298.15 K] = \Delta H_m^0 (1a) - 7\Delta H_m^0 [H_2O(l), 298.15 K] 
+ 2\Delta H_m^0 [C_{12}H_8N_2 \cdot H_2O(s), 298.15 K] + \Delta H_m^0 [\text{Bi(NO}_3)_3 \cdot 5H_2O(s), 298.15 K] 
= \left[ (-30.18) - 7 \times (-285.83) + 2 \times (-391.34) + (-1986.87) \right] \]
\[ \pm \sqrt{(0.51)^2 + (7 \times 0.04)^2 + (2 \times 2.98)^2 + (0.20)^2} \]
\[ = -(798.92 \pm 5.99) \text{ kJ mol}^{-1} \]

**Microcalorimetry**

*Thermogenic curves*

The thermogenic curves for growth of *S. pombe* treated by different concentrations of the complex were determined using the ampoule method at 32.00 °C, respectively. All microcalorimetric experiments were performed in triplicates. The power–time curves are illustrated in Fig. 6. From Fig. 6, the metabolic process could be divided into four phases: lag phase, log (exponential) phase, stationary phase, and decline phase [15, 16].

*Thermokinetics*

During the log phase, the power–time curves obey the following equation [25]:
\[\ln P_t = \ln P_0 + kt - kt_0 \tag{6}\]
where \(P_0\) and \(P_t\) stand for the heat–output power at the beginning of baseline and at time \(t\), respectively; \(k\) is the growth rate constant of *S. pombe* at specified condition, whose size represents growth speed. So using the data \(P_t\) and \(t\) taken from the power–time curves to fit Eq. (6), the growth rate constant \(k\) values of *S. pombe* at different concentrations were obtained via linear fitting with the computer (Table 3). As is shown in Table 3, the growth rate constant \(k\) decreased with the increase in concentration of the drug. The inhibition ratio of the growth metabolism of *S. pombe* by drug is defined as the following:
\[I = \frac{(k_0 - k_c)}{k_0} \times 100\% \tag{7}\]
where \(k_0\) is the rate constant of the control and \(k_c\) is the rate constant under an inhibitor with a concentration of \(c\). The values of \((I)\) were shown in Table 3. Plotting the inhibition ratio \((I)\) against the concentration \((c)\) of the complex is shown Fig. 7. As can be seen from the figure, the inhibition ratio \((I)\) was gradually increased with the increase in concentration of the complex, which indicated the growth of *S. pombe* was significantly inhibited. Using the logistic curve fitting from data of the inhibition ratio \((I)\) of *S. pombe* with concentration \((c)\) of the complex, the curve equation was obtained:
\[I = 84.76 - \frac{85.69}{1 + \left(\frac{c}{0.025}\right)^{551}} \tag{8}\]
(1.5 × 10⁻⁵ mol L⁻¹ ≤ \(C_{(\text{the complex})}\) ≤ 3.8 × 10⁻⁵ mol L⁻¹).

The correlation coefficient \(R\) was 0.9767. Thus, the inhibition ratio in the range of the above applied amount of the complex on *S. pombe* could be clearly inferred through the application of Eq. (8). When the inhibition ratio was 50%, the drug concentration was the half inhibition concentration \((IC_{50})\). The half inhibition concentration \((IC_{50})\) of the complex was found to be 2.8 × 10⁻⁵ mol L⁻¹.
Thermodynamics

The total thermal effects ($Q_{\text{total}}$) value can be calculated by the area under the power–time curves, and listed in Table 3. Drawing the total thermal effects ($Q_{\text{total}}$) of *S. pombe* growth against concentration ($c$), the curve was shown in Fig. 8. Using the logistic curve fitting from data of the total thermal effects ($Q_{\text{total}}$) of *S. pombe* growth with the concentration of the complex, the curve equation was obtained:

$$Q_{\text{total}} = 13.82 + \frac{71.30}{1 + \left(\frac{c}{0.022}\right)^{3.49}}$$  \hspace{1cm} (9)

$$(1.5 \times 10^{-5} \text{ mol L}^{-1} \leq C_{(\text{the complex})} \leq 3.8 \times 10^{-5} \text{ mol L}^{-1}).$$

The correlation coefficient $R$ was 0.9949. Thus, the total thermal effects in the range of the above applied amount of the complex on *S. pombe* could be clearly inferred through the application of Eq. (9). From Fig. 8, it could be seen that the total thermal effects ($Q_{\text{total}}$) of *S. pombe* growth decreased with increase in the concentration of the complex, which indicated that the complex significantly inhibited the growth of *S. pombe* cell. This is mainly because after addition of the drug into the *S. pombe* suspension, some cells were inhibited or killed, but the survivors continue to metabolize which maintain a lower level of the heat production rate, and this level is directly depending on the drug concentration.

![Fig. 7 Relationship between the concentration of the complex and the growth inhibition rate (I) of *S. pombe*](image)

![Fig. 8 Total thermal effects ($Q_{\text{total}}$) of *S. pombe* with different concentrations of the complex](image)

Table 3  Thermokinetics parameters of *S. pombe* growth affected by the inhibitor at different concentrations

<table>
<thead>
<tr>
<th>Inhibitors</th>
<th>$C_a/(10^{-3} \text{ mol L}^{-1})$</th>
<th>$K_b/\text{min}^{-1}$</th>
<th>$I_c/%$</th>
<th>$IC_{50}/\text{mol L}^{-1}$</th>
<th>$Q_{\text{total}}/\text{J}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>The complex</td>
<td>0.000</td>
<td>$6.18 \times 10^{-5} \pm 2.69 \times 10^{-8}$</td>
<td>0</td>
<td>$2.8 \times 10^{-5}$</td>
<td>84.89</td>
</tr>
<tr>
<td></td>
<td>0.015</td>
<td>$6.12 \times 10^{-5} \pm 2.06 \times 10^{-8}$</td>
<td>0.97</td>
<td>71.17</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.019</td>
<td>$5.21 \times 10^{-5} \pm 2.72 \times 10^{-8}$</td>
<td>15.6</td>
<td>55.45</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.023</td>
<td>$4.13 \times 10^{-5} \pm 3.35 \times 10^{-8}$</td>
<td>33.2</td>
<td>47.38</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.027</td>
<td>$3.52 \times 10^{-5} \pm 1.87 \times 10^{-8}$</td>
<td>43.0</td>
<td>37.52</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.031</td>
<td>$1.97 \times 10^{-5} \pm 1.47 \times 10^{-8}$</td>
<td>68.1</td>
<td>29.55</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.035</td>
<td>$1.68 \times 10^{-5} \pm 1.03 \times 10^{-8}$</td>
<td>72.8</td>
<td>26.03</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.038</td>
<td>$1.61 \times 10^{-5} \pm 1.89 \times 10^{-8}$</td>
<td>73.9</td>
<td>22.57</td>
<td></td>
</tr>
</tbody>
</table>

* a The concentration
* b The growth rate constant of *S. pombe*
* c The inhibitive ratio
* d The half inhibition concentration
* e Mean ± SD; $n = 3$
Conclusions

In this work, a bismuth(III) complex \([\text{C}_{12}\text{H}_{8}\text{N}_{2}]_{2}\text{Bi(O}_{2}\text{NO})_{3}]\) was prepared and characterized. According to the principles of thermodynamics, the standard molar enthalpies of formation of the complex and Bi(NO\(_3\))\(_3\), Si-H, O-H, and N-H were estimated to be \(\Delta H^0_m\) \([\text{C}_{12}\text{H}_{8}\text{N}_{2}]_{2}\text{Bi(O}_{2}\text{NO})_{3}] = -(798.92 \pm 5.99)\) kJ mol\(^{-1}\) and \(\Delta H^0_m\) [Bi(NO\(_3\))\(_3\):Si-H,O,H,N] = -(1986.87 \pm 0.20)\) kJ mol\(^{-1}\), respectively. The microcalorimetric method was used to study the influence of synthetic complex on the growth of \(S.\) \(pombe\). The thermokinetic parameters of growth, such as growth rate constants \(k\), the inhibition ratio \(I\) and half inhibition concentration IC\(_{50}\) were obtained. The quantitative relationships of the \(I\) and \(Q\) values of \(S.\) \(pombe\) with concentrations of the complex were discussed. IC\(_{50}\) value of the complex was found to be \(2.8 \times 10^{-5}\) mol L\(^{-1}\), which indicated that the complex had good bioactivity on the growth metabolism of \(S.\) \(pombe\) [15]. Moreover, the present work has also demonstrated that microcalorimetry is a valuable tool to evaluate the biological activity of drugs because it could provide important thermokinetics and thermodynamic information that cannot be obtained from conventional biological techniques [13]. In conclusion, this work provides some important reference data, which may benefit the research of bismuth complexes.

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