

Synthesis, spectral characterisation and thermal studies of zirconyl complexes of biologically active molecules

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Abstract Zirconyl complexes of hippuric acid ($C_9H_9NO_3$, hipH) and monophenylbutazone (4-butyl-1-phenyl-3,5-pyrazolidinedione, MPB) were prepared using $ZrOCl_2 \cdot 8H_2O$ and $ZrO(NO_3)_3 \cdot xH_2O$ and characterized by elemental analysis, molar conductance measurement and IR, UV–Vis and NMR spectral methods. Thermal decomposition behaviour was studied by thermogravimetry. The second harmonic generation (SHG) conversion efficiency of hippuric acid complexes was also studied.

Keywords Hippuric acid · 1H NMR · IR · Monophenylbutazone · SHG · Thermal studies · Zirconyl complexes

Introduction

Hippuric acid, *N*-benzoylglycine, is one of the amino acid found in herbivorous animals and humans. Hippuric acid is potentially capable of forming coordinate bonds with many metal ions through carboxylic oxygen atoms as a bidentate ligand [1–12].

Monophenylbutazone belongs to the family of non-steroidal anti-inflammatory drugs [13, 14] (NSAID). The ligand exhibits keto-enol tautomerism which may be expected to show various bonding and stereo chemical behaviour [15].

The present investigation was undertaken to study zirconyl complexes of hippuric acid (Fig. 1) and monophenylbutazone (Fig. 2).

Experimental methods

All chemicals used were of AR or GR grade and used as such. Monophenylbutazone was purchased from Sigma Company (USA). Hippuric acid and metal salts were procured from CDH.

Carbon, nitrogen and hydrogen were determined using Vario EL 111 CHNS analyzer. The metal contents were found gravimetrically by converting the compounds into ZrO_2 .

The IR spectra were recorded on Thermo Nicolet Avtar 310 DTGS spectrometer ($4000\text{--}400\text{ cm}^{-1}$) in KBr pellets. UV–Vis spectra were recorded in methanol for ligands and DMF for complexes using Varian Cary 5000 spectrometer with 1 cm quartz cell, in the range 200–800 nm. Molar conductivity of complexes in methanol and DMF ($\sim 1 \times 10^{-3}\text{ mol dm}^{-3}$) were measured using Systronics Conductivity Meter 304.

1H NMR of MPB and its complexes were carried out in methanol solvent using Joel GSX 400 FT-NMR Spectrometer.

The SHG efficiency of hippuric acid and complexes were measured with respect to KDP by powder technique developed by Kurtz and Perry [16] using a Quanta Ray Spectra Physics Model: Prolab 170 Nd: YAG 10 ns laser with first harmonic output of 1064 nm at the pulse repetition rate 10 Hz. The homogenous powder was tightly packed in a microcapillary tube and mounted in the path of laser beam of pulse energy 2.4 mJ obtained by split beam technique.

Thermo gravimetric analysis (TG, DTG) was carried out in air with a heating rate of $10\text{ }^\circ\text{C}/\text{min}$ using Perkin Elmer Diamond TG/DTG analyser.

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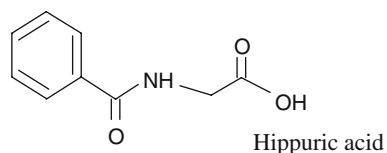


Fig. 1 Hippuric acid

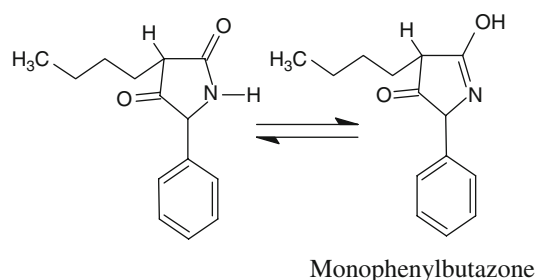


Fig. 2 Monophenylbutazone

Synthesis of metal complexes

Synthesis of [ZrO(hip)(OH)H₂O]

Sodium salt of hippuric acid (0.3 g, 1.67 mmol) was prepared in 0.1 M NaOH (pH ~ 7). A slight excess of the ligand was taken to exclude the excess alkali. The resulting suspension was filtered. To the clear solution, zirconyl nitrate (3.9 mL, 1.67 mmol) at pH ~ 3–4 was added drop wise with stirring. The white precipitate formed was filtered, washed several times with distilled water and dried.

Synthesis of [ZrO(hipH)₄Cl₂]

A similar procedure was used. Here hippuric acid (0.3 g, 1.67 mmol) and zirconyl chloride (9.6 mL, 0.4175 mmol) were used.

Synthesis of [ZrO(MPB)₃(OH)₂]

Sodium salt of monophenylbutazone, (0.3 g, 1.3 mmol) was prepared in 0.1 M NaOH (pH ~ 7). Here also slight excess of the ligand was taken to exclude the excess alkali. The suspension was filtered. To this solution zirconyl

nitrate reagent (0.9 mL, 0.4 mmol) pH ~ 3–4, was added drop wise with stirring. The precipitate formed was filtered, washed with distilled water and dried.

Synthesis of [ZrOCl₂(MPB)₄]

A similar procedure was followed. Here monophenylbutazone (0.3 g, 1.3 mmol) and zirconyl chloride reagent [3.6 mL, 0.7 mmol] was taken.

Results and discussion

The complexes are air stable. Hippuric acid complexes are insoluble in water and most of the organic solvents, and soluble in DMF. The elemental analysis data and proposed composition are given in Table 1.

Molar conductance measurements

The molar conductivity value of hippuric acid complexes in DMF ($\sim 1 \times 10^{-3}$ mol dm⁻³) and MPB complexes in methanol ($\sim 1 \times 10^{-3}$ mol dm⁻³) are shown in Table 1. The conductance values are in the range expected for non-electrolytes.

Infrared spectra

The main IR spectral bands of hippuric acid (hipH) and its complexes and their tentative assignments are summarized in Table 2.

In the case of [ZrO(hip)(OH)H₂O] complex, $\nu(\text{O-H})$ of the coordinated hydroxyl group, $\nu(\text{O-H})$ of water molecule and $\nu(\text{N-H})$ merge together and shown as a broad band in the region 3300–3400 cm⁻¹. The strong band at 1744 cm⁻¹ due to $\nu(\text{C=O})$ of carboxylic acid group is absent in [ZrO(hip)(OH)H₂O] indicates that hippuric acid coordinates to the metal ion through carboxylate group [17, 18]. The asymmetric stretching of carboxylate group at 1576 cm⁻¹ and symmetric stretching at 1403 cm⁻¹ support this. The above observations support the bidentate coordination of hippurate. There is no apparent shift for the band at 1744 cm⁻¹

Table 1 Analytical data of complexes

Sl. No	Complexes	Colour	C	H	N	Molar conductance/ $\Omega^{-1} \text{ cm}^{-1} \text{ mol}^{-1}$
1	[ZrO(hip)(OH)H ₂ O]	White	33.70 (34.35)	3.4 (3.95)	4.36 (4.48)	10.5
2	[ZrO(hipH) ₄ Cl ₂]	White	48.31 (47.33)	3.69 (4.58)	6.25 (6.14)	21
3	[ZrO(MPB) ₃ (OH) ₂]	Yellow	55.87 (55.10)	5.97 (4.05)	10.02 (9.33)	4
4	[ZrO(MPB) ₄ Cl ₂]	Yellow	56.38 (55.92)	5.42 (6.29)	10.11 (9.94)	5

Table 2 IR spectral data of hippuric acid and its complexes

Hippuric acid	[ZrO(hip)(OH)]H ₂ O	[ZrO(hipH) ₄ Cl ₂]	Assignments
	3300–3400(b)		$\nu(\text{O-H}), \text{H}_2\text{O} + \nu(\text{O-H}) + \nu(\text{N-H})$
3342(s)		3342(s)	$\nu(\text{N-H})$
3073	3073	3073	Aromatic $\nu(\text{C-H})$
2750–2478 (several bands)		2750–2478	$\nu(\text{O-H})$ in COOH
1744(s)		1745(s)	$\nu(\text{C=O})$; COOH
1600(s)	1603(s)	1600(s)	$\nu(\text{C=O})$; benzoyl
	1576(s)		$\nu_{\text{as}}(\text{COO}^-)$
	1403(s)		$\nu_{\text{s}}(\text{COO}^-)$
	481	485	$\nu(\text{Zr-O})$

assigned to $\nu(\text{C=O})$ of COOH group in [ZrO(hipH)₄Cl₂]. Several bands due to carboxylic OH (2750–2478 cm⁻¹) also remain in the complex. These observations confirm the neutral coordination of hippuric acid in the complex formed. The bands at 481 cm⁻¹ and 485 cm⁻¹ in the complexes are assigned to $\nu(\text{Zr-O})$ of [ZrO(hip)(OH)]H₂O and [ZrO(hipH)₄Cl₂], respectively [19].

The important IR spectral bands of monophenylbutazone and its complexes and their tentative assignments are summarized in Table 3.

The bands at 1729 and 1685 cm⁻¹ in the free ligand are assigned to the stretching of the tautomeric and non-tautomeric carbonyl groups, respectively [15]. The IR spectrum of the ligand also shows a medium band around 3308 cm⁻¹. This is assigned to the N–H stretching of amide band. In the complexes there is no shift for the peaks at 1685 cm⁻¹. But the band at 1729 cm⁻¹ is shifted to 1737 and 1745 cm⁻¹ in [ZrO(MPB)₃(OH)₂] and [ZrOCl₂(MPB)₄], respectively. The upward shift arises from the release of carbonyl group from hydrogen bonding. The band at 3381 cm⁻¹ is assigned to the $\nu(\text{O-H})$ of the coordinated hydroxyl group in [ZrO(MPB)₃(OH)₂]. The bands at 600 and 581 cm⁻¹ are assigned

Table 3 The IR spectral data of monophenylbutazone and its complexes

MPB	[ZrO(MPB) ₃ (OH) ₂]	[ZrOCl ₂ (MPB) ₄]	Assignments
	3381(b)		$\nu(\text{O-H})$
3308(s)	3306(s)	3307	$\nu(\text{N-H})$
3069(s)	3060(s)	3066	aryl $\nu(\text{C-H})$
2956	2958	2958	Saturated $\nu(\text{C-H})$
1729(s)	1737(s)	1745(s)	$\nu_{\text{as}}(\text{C=O})$; tautomeric
1685(s)	1686(s)	1688(s)	$\nu_{\text{as}}(\text{C=O})$; non-tautomeric
1597	1596	1596	$\delta(\text{N-H})$ bending
	600	581	$\nu(\text{Zr-O})$

to the $\nu(\text{Zr-O})$ of the complexes [ZrO(MPB)₃(OH)₂] and [ZrO(MPB)₄Cl₂], respectively. Thus MPB act as a monodentate ligand coordinating through tautomeric carbonyl group in the complexes.

¹H NMR spectra

The NMR spectrums of the ligands are well reproduced in the spectrum of the complexes with only minor changes. The N–H of MPB is not observed in the range of measurement used.

Electronic spectra

The electronic spectra for hippuric acid in methanol and its complexes in DMF and monophenylbutazone and its complexes in MeOH show ligand transitions only and did not show any d–d transitions as expected.

Second harmonic generation efficiency

The SHG measurement was carried out for the complexes of hippuric acid. The SHG outputs are given in Table 4. The data show that the chloro complexes have six times efficiency than that of hydroxo complexes.

Thermal behaviour of complexes

The thermal analysis curves (TG and DTG) of the hippuric acid complexes are given in Figs. 3 and 4.

Table 4 Measured SHG values of metal complexes of hippuric acid

Sample	SHG signal/mV	Efficiency
[ZrO(hip)(OH)]H ₂ O	18	0.04
[ZrO(hipH) ₄ Cl ₂]	98	0.24
KDP	410	1

The thermal decomposition of all the complexes was taken in air at a heating rate of 10 °C/min. For the complex [ZrO(hip)(OH)H₂O], the decomposition occurs in five stages, as shown by five DTG peaks. The final mass of the residue corresponds to ZrO₂ [20]. The kinetic parameters were calculated for three clear cut stages using Coats-Redfern [21] (I), MacCallum-Tanner [22] (II) and Madusudhanan Krishnan Ninan's (III) equations and are summarized in Table 5.

For the complex [ZrO(hipH)₄Cl₂], in air the decomposition occurs in two stages, kinetic parameters calculated for these two stages are given in Table 6.

The thermal analysis curves of MPB and its complexes are given in Figs. 5 and 6.

The thermal decomposition of the complexes [ZrO(MPB)₃(OH)₂] and [ZrO(MPB)₄Cl₂] take place in two stages as shown by two DTG peaks. The kinetic parameters are also calculated for the distinct stages and are

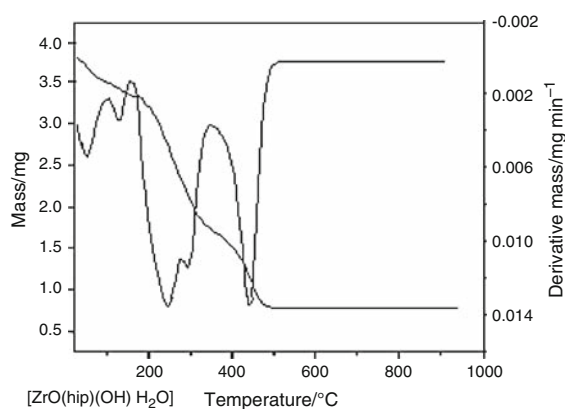


Fig. 3 TG and DTG curves of [ZrO(hip)(OH)H₂O] in air

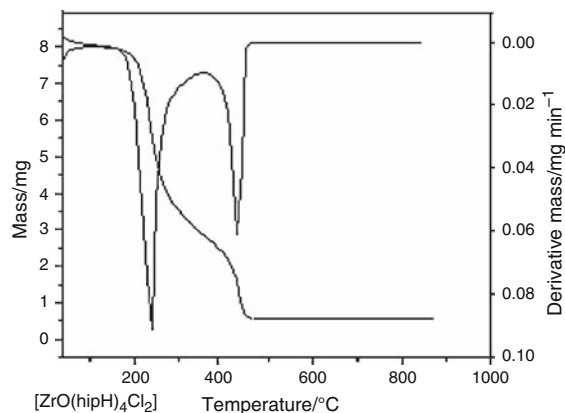


Fig. 4 TG and DTG curves of [ZrO(hipH)₄Cl₂] in air

Table 5 Kinetic parameters of the complex [ZrO(hip)(OH)H₂O] in air

Stages	Methods	<i>n</i>	<i>E</i> / kJ mol ⁻¹	ΔS / J K ⁻¹ mol ⁻¹	log <i>A</i> / s ⁻¹	<i>r</i>
1	I	1.5	25.08	-221.98	1.67	0.986466
	II	1.5	29.19	-215.91	1.98	0.980324
	III	1.5	28.98	-217.60	1.89	0.979999
3	I	0.9	135.31	-2.41	13.13	0.990424
	II	0.9	138.42	-6.20	13.58	0.988390
	III	0.9	135.35	-1.36	13.19	0.989431
5	I	1.8	140.26	-23.62	12.02	0.997766
	II	1.8	139.41	-24.03	12.00	0.997547
	III	1.8	139.19	-24.92	11.96	0.997501

r Correlation coefficient

Table 6 Kinetic parameters of the complex [ZrO(hipH)₄Cl₂] in air

Stages	Methods	<i>n</i>	<i>E</i> / kJ mol ⁻¹	ΔS / J K ⁻¹ mol ⁻¹	log <i>A</i> / s ⁻¹	<i>r</i>
1	I	1	110.30	-81.88	8.98	0.998723
	II	1	110.23	-80.84	9.04	0.998588
	III	1	110.02	-81.82	8.99	0.998581
2	I	0.9	60.55	-212.33	2.17	0.960078
	II	0.9	58.40	-216.87	1.93	0.946836
	III	0.9	58.04	-218.49	1.85	0.946156

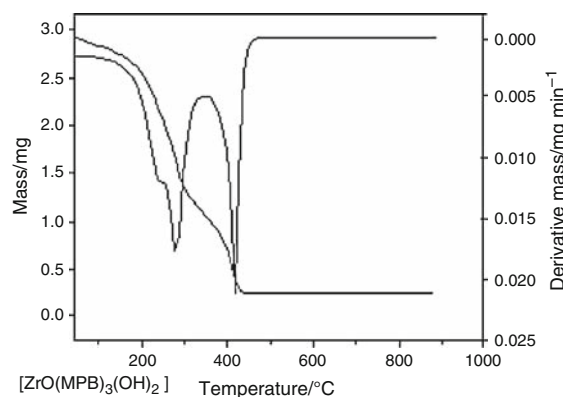


Fig. 5 TG and DTG curve of [ZrO(MPB)₃(OH)₂] in air

summarized in Tables 7 and 8. The negative ΔS value of the decomposition stages show that the complexes are more ordered in the activated state than the reactant and the reactions are slower than normal [23, 24]. Entropy of activation follows no definite trend.

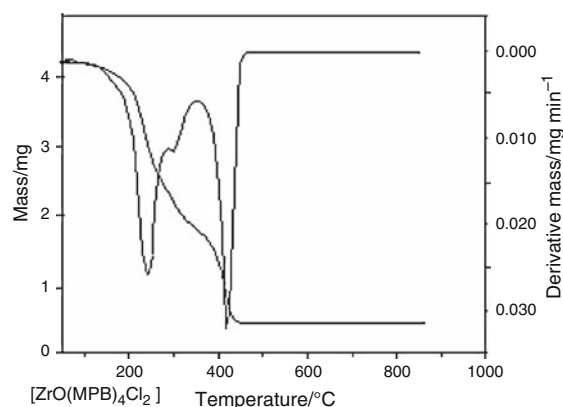


Fig. 6 TG and DTG curves of $[\text{ZrO}(\text{MPB})_4\text{Cl}_2]$ in air

Table 7 Kinetic parameters of the complex $[\text{ZrO}(\text{MPB})_3(\text{OH})_2]$ in air

Stages	Methods	<i>n</i>	<i>E</i> / kJ mol ⁻¹	ΔS / J K ⁻¹ mol ⁻¹	log <i>A</i> / s ⁻¹	<i>r</i>
1	I	0.9	18.92	-264.79	-0.57	0.973304
	II	0.9	20.54	-269.00	-0.79	0.959331
	III	0.9	20.28	-271.09	-0.90	0.958479
2	I	0.9	97.02	-154.78	5.17	0.985213
	II	0.9	94.51	-158.47	4.98	0.982118
	III	0.9	94.18	-159.76	4.91	0.981961

Table 8 Kinetic parameters of the complex $[\text{ZrO}(\text{MPB})_4\text{Cl}_2]$ in air

Stages	Method	<i>n</i>	<i>E</i> / kJ mol ⁻¹	ΔS / J k ⁻¹ mol ⁻¹	log <i>A</i> / s ⁻¹	<i>r</i>
1	I	0.9	50.39	-197.07	2.97	0.993648
	II	0.9	51.40	-196.12	3.02	0.992107
	III	0.9	51.15	-197.58	2.94	0.992021
2	I	0.9	35.46	-247.33	0.34	0.962449
	II	0.9	34.13	-253.35	0.03	0.940292
	III	0.9	33.76	-255.32	-0.08	0.939027

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References

- Capllonch MC, Garcia-Raso A, Terron A, Apella MC, Espinosa E, Molins E. Interactions of d10 metal ions with hippuric acid and cytosine X-ray structure of the first cadmium (II)-amino acid derivative-nucleobase ternary compound. *J Inorg Biochem.* 2001;85:173–8.
- Sgarabotto P, Bisceglie F, Pelosi G, Abdel-Rahman L. Synthesis, x-ray crystal structures and characterization of copper(II)-2,2'-bipyridyl derivatives of (4-amino)-hippuric acid and of L-proline. *Polyhedron.* 1999;8:2505–10.
- Terron A, Fiol JJ, Herrero LA, Garcia-Raso A, Apella MC, Caubet A, et al. Metal-amino acid (or peptide)-nucleoside (or related bases) ternary complexes. *An Quim Int Ed.* 1997;93:60–7.
- Garcia-Raso A, Fiol JJ, Adrover B, Moreno V, Molins E, Mata L. Synthesis and structure of isocytosine ternary copper(II) complexes. *Dalton Trans J Chem Soc.* 1998;1031–6.
- Ashby CIH, Paton WF, Brown TL. Nitrogen-14 nuclear quadrupole resonance spectra of the coordinated amino group and of coordinated imidazole. Crystal and molecular structures of chloroglycylglycinato(imidazole)cadmium. *J Am Chem Soc.* 1980;102:2990–8.
- Morelock MM, Good ML, Trefonas LM, Karraker DG, Maleki L, Eichelberger HR, et al. Metal ion complexes of alpha amino acids. Structure and magnetic properties of the nickel and cobalt hippurates. Pseudo-one-dimensional magnetic systems. *J Am Chem Soc.* 1979;101:4858–66.
- Grewe H, Udupa MR, Kerbs B. Crystal and molecular structure of bis(N-benzoylglycinato)triaquozinc(II) dihydrate. *Inorg Chim Acta.* 1982;63:119–24.
- Brzyska W, Hakim M. Thermal decomposition of Co(II), Ni(II), Cu(II) and Zn(II) hippurates. *J Therm Anal Calorim.* 1990;36:847–53.
- Brzyska W, Hakim M. Thermal decomposition of Y, La and light lanthanide complexes of hippuric acid. *J Therm Anal.* 1988;34:47–53.
- Refat MS, Teleb SM, Sadeek SA, Khater HM, El-Megharbel SM. Synthesis and characterization of some hippurate rare earth metal complexes. *J Kor Chem Soc.* 2005;49:3261–68.
- Sadeek SA, Refat MS, Teleb SM, Megharbel EI. Synthesis and characterization of V(III), Cr(III) and Fe(III) hippurates. *J Mol Struct.* 2005;737:139–45.
- Allan JR, Dalrymple J. The thermal, spectral and magnetic studies of hippuric acid compounds of cobalt (II), nickel (II), copper (II) and zinc (II) ions. *Thermochim Acta.* 1991;185:83–9.
- Khayyal MT, El-Ghazaly M, El-Khatib AS, Hatem A. Tolerability of mofebutazone in asthmatic patients. *Int J Clin Pharmacol Res.* 1995;15:145–51.
- Paradies HH, Ziedrich KH, Hans H, Flaeming. Zur-keto-enol-tomerie von 1-phenyl 4n-butyl-pyrazolidin-(3,5)dion. *Acta Pharm Technol.* 1987;33:180–8.
- Suma S, Sudarsanakumar MR, Nair CGR, Prabhakaran CP. Synthesis and characterization of chromium(III), manganese(III), iron(III), cobalt(II), nickel(II), copper(II), zinc(II), cadmium(II) and mercury(II) complexes of monophenylbutazone. *Indian J Chem.* 1994;33A:1107–9.
- Kurtz SK, Perry TT. A powder technique for the evaluation of nonlinear optical materials. *J Appl Phys.* 1968;39:3798–813.
- Kumar G, Srivastava M. Spectral and magnetochemical studies of nickel(II) and cobalt(II) complexes of hippuric acid. *Rev Chim Miner.* 1979;16:14–8.
- Nakamoto K. Infrared and Raman spectra of inorganic and coordination compounds. 4th ed. New York: Wiley; 1986.
- Refat MS, EI Korashy SA, Ahmed S. Synthesis and characterization of Mn(II), Au(III) and Zr(IV) hippurates complexes. *Spectrochim Acta Part A Biomol Spectrosc.* 2008;70:840–9.
- Drożdż-Cieśla E, Małecki A. Mechanism of thermal decomposition of zirconyl oxalate ZrOC_2O_4 . *J Therm Anal Calorim.* 2008;92:939–44.
- Coats AW, Redfern JP. Kinetic parameters from thermogravimetric data. *Nature.* 1964;201:68–9.
- MacCallum JR, Tanner. The kinetics of thermogravimetry. *J Eur Polym.* 1970;6:1033–7.
- Muraleedharan Nair MK, Radhakrishnan PK. Thermal decomposition kinetics of lanthanum complexes of 1,2-(Diimino-4'-Antipyrinyl)ethane. *Thermochim Acta.* 1997;292:115–22.
- Thankamony M, Sindhu Kumari B, Rijulal G, Mohanan K. Lanthanum(III) chloride complexes with heterocyclic Schiff bases. *J Therm Anal Calorim.* 2009;95:259–66.