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Thermal and spectroscopic studies on solid ibuprofen complexes of lighter trivalent lanthanides

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ABSTRACT

Solid-state compounds of general formula $Ln(L)_3$, in which L is ibuprofen and Ln stands for trivalent La, Ce, Pr, Nd, Sm and Eu, have been synthesized. Simultaneous thermogravimetry and differential thermal analysis (TG-DTA), X-ray powder diffractometry (DRX), complexometry, Fourier-transformed infrared spectroscopy (FTIR) and thermogravimetry coupled to Fourier-transformed infrared spectroscopy (TG-FTIR) were used to characterize these compounds. The results provided information concerning the chemical composition, dehydration, coordination modes of the ligands, crystallinity of the samples, thermal behavior and thermal decomposition of the compounds. The theoretical and experimental spectroscopic studies suggest that ibuprofen coordinates through the carboxylate group as a chelating ligand.

1. Introduction

Thermal methods of analysis are widely used to investigate polymorphism, thermal decomposition, thermal stability [1–4], solid state reactions, drug formulations [5–7], purity [8], reaction kinetics [9], evolved gas analysis by coupled TG-FTIR [10] and other properties of solid compounds used in pharmaceutical industry [11]. Due to the numerous researches directly and indirectly involved with these issues, it is essential to have a complete understanding of the properties of pharmaceutical materials.

Ibuprofen, or (*RS*)-2-(4-(2-methylpropyl)phenyl)propanoic acid, is a non-steroidal anti-inflammatory drug (NSAID) that belongs to the class of 2-arylpropionic acids, which constitute a considerable group of pharmaceutical and commercial interest (Fig. 1). From the pharmacological standpoint, the 2-arylpropionic acids act by blocking the conversion of arachidonic acid into prostaglandins and thromboxane A2, which are responsible for the inflammatory mechanism through inhibition of cyclooxygenase [12].

The lanthanides show widely diverse coordination compounds. These compounds often possess remarkable and unique spectroscopic, photophysical and electrochemical properties that can be explored in applications for sensory, pharmacology and diagnostic [13–16]. Complexes of ketoprofen – another NSAID – with lighter [17] and heavier [18] lanthanides were synthesized and characterized by our group. The motivation for the preparation of lanthanide complexes with NSAIDs is the structural similarity with other lanthanide complexes already reported in the literature that showed pharmacological, diagnostic and therapeutic applications [16]. In this sense, this work's purpose is to provide groundwork for future pharmacological applications.

2. Experimental

Ibuprofen (acid form) with ≥98% purity was purchased from Aldrich. An aqueous solution of ibuprofen sodium salt (0.1 mol L^{-1}) was prepared by neutralizing an aqueous ibuprofen suspension with a 0.1 mol L^{-1} sodium hydroxide solution and the pH was adjusted to 8.0. Lanthanide chlorides were prepared from the corresponding metal oxides (except for cerium) by treatment with concentrated hydrochloric acid. The resulting solutions were evaporated to near dryness by heating and the remaining residues were redissolved in distilled water and the solutions were once again evaporated to near dryness to eliminate the excess of hydrochloric acid. The residues were finally dissolved in distilled water, transferred to a volumetric flask and diluted in order to obtain ca. 0.1 mol L^{-1} solutions, whose pH's were adjusted to 5.0 by adding

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Table 1
Analytical data for $Ln(L)_3 \cdot nH_2O$.

Compound	Metal (%)			L (lost) (%)		Water (%)		Final residue (%)		
	Calc.	TG	EDTA	Calc.	TG	Calc.	TG	Calc.	TG	Oxide
$La(L)_3 \cdot H_2O$	17.97	18.17	18.38	76.58	76.06	2.33	2.63	21.08	21.31	La_2O_3
$Ce(L)_3 \cdot H_2O$	18.10	18.73	18.73	75.42	74.21	2.33	2.78	22.24	23.01	CeO_2
$Pr(L)_3 \cdot H_2O$	18.19	19.17	18.45	75.69	73.97	2.33	2.85	21.99	23.18	Pr_6O_{11}
$Nd(L)_3 \cdot H_2O$	18.54	17.90	18.31	76.05	77.20	2.32	1.93	21.62	20.87	Nd_2O_3
$Sm(L)_3 \cdot H_2O$	19.17	19.70	19.28	75.46	74.87	2.30	2.28	22.23	22.85	Sm_2O_3
$Eu(L)_3 \cdot 1.5H_2O$	19.12	18.55	19.59	74.45	75.83	3.40	2.69	22.14	21.48	Eu_2O_3

L = ibuprofen.

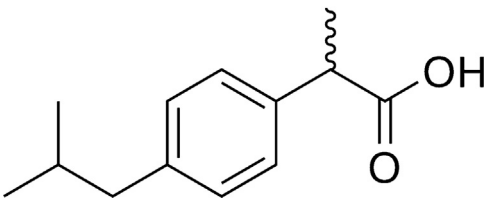

Fig. 1. Structural formula of ibuprofen.

diluted sodium hydroxide or hydrochloric acid solutions. Cerium (III) was used as nitrate and ca. 0.1 mol L^{-1} aqueous solutions were prepared by direct weighing and dissolution of the salt.

The complexes were prepared by adding, slowly and under continuous stirring, solutions of ibuprofen sodium salt to the respective metal chloride or nitrate solutions until total precipitation of the complexes. The precipitates were filtered through a Whatman no 42 filter paper, washed with distilled water in order to eliminate the chloride or nitrate ions and kept in a desiccator over anhydrous calcium chloride under reduced pressure.

Simultaneous TG-DTA curves were obtained with a SDT 2960 (TA Instruments) thermal analysis equipment, under the following experimental conditions: open α-alumina crucibles, heating rate of 20 °C min^{-1}, air atmosphere flow of 100 mL min^{-1} and samples of about 5 mg.

The metal contents were determined by complexometric titrations with standard EDTA solution using xylenol orange as indicator [19].

X-ray powder diffractograms were measured on a Siemens D-5000 X-ray diffractometer using Cu Kα radiation (λ = 1.541 Å) and settings of 40 kV and 20 mA.

The measurements of the gaseous products were carried out using a TGA/DSC 1 STAR^e System from Mettler Toledo coupled to a Nicolet FTIR spectrophotometer with gas cell and DTGS KBr detector. The furnace and the heated gas cell (250 °C) were coupled through a heated (200 °C) 120 cm stainless steel line transfer with diameter of 3 mm purged with dry air (50 mL min^{-1}). The FTIR spectra were recorded with 16 scans per spectrum and resolution of 4 cm^{-1}.

The DSC curve of the neodymium complex was obtained on a Q-10 thermal analysis system (TA Instruments) under the following experimental conditions: aluminum crucible with perforated cover, heating rate of 10 °C min^{-1}, air atmosphere flow of 100 mL min^{-1} and sample of about 3 mg.

The attenuate total reflectance infrared spectra were run on a Nicolet iS10 FTIR spectrophotometer using an ATR accessory with Ge window within the 4000–600 cm^{-1} range.

3. Computational strategy

In this study, the employed quantum chemical approach used to determine the molecular structures was the Becke three-parameter hybrid theory [20] using the Lee–Yang–Par (LYP) correlation functional [21] and the basis sets used for the calculations were: 4s for H (^{2}S) [22], [5s4p] for C (^{3}P) and O (^{3}P) [22] and [17s11p7d] for La (^{2}D) [23]. The diffuse functions for the lanthanum atom (^{2}D) were calculated according to the procedure described in reference [23] and these values are: $\alpha s = 0.00669534$, $\alpha p = 0.079333735$, $\alpha d = 0.096432865$. In order to better describe the properties of the compound in the implementation of the calculations, it was

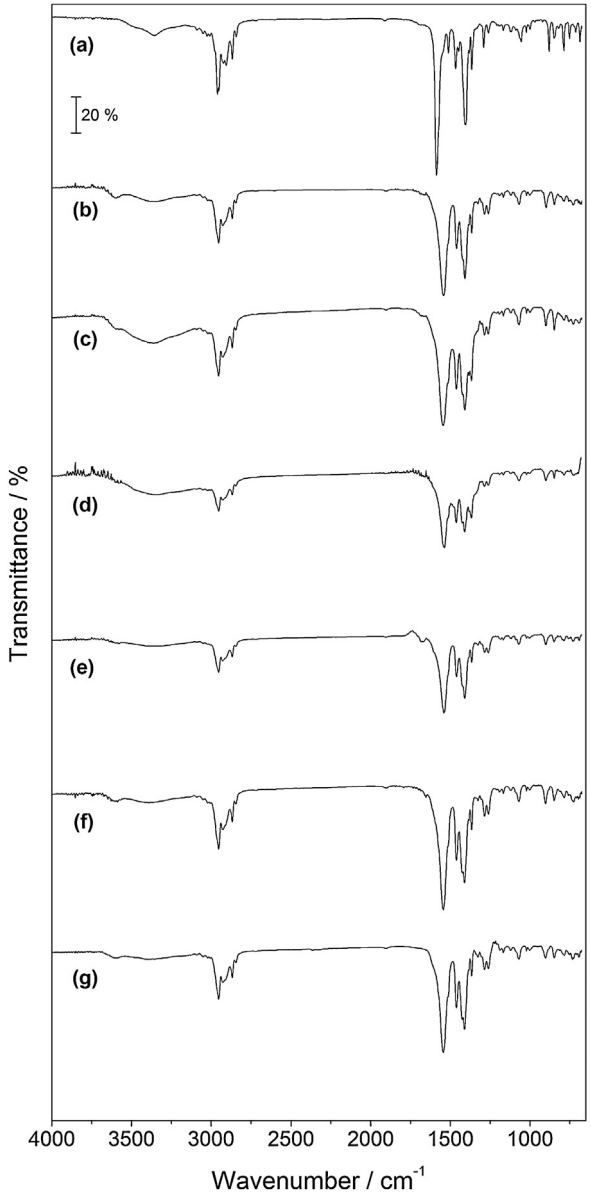

Fig. 2. Attenuate total reflectance infrared spectra of (a) $NaL \cdot 0.5H_2O$, (b) $La(L)_3 \cdot H_2O$, (c) $Ce(L)_3 \cdot H_2O$, (d) $Pr(L)_3 \cdot H_2O$, (e) $Nd(L)_3 \cdot H_2O$, (f) $Sm(L)_3 \cdot H_2O$ and (g) $Eu(L)_3 \cdot 1.5H_2O$.