Polyhedron 80 (2014) 117–128

Contents lists available at ScienceDirect

Polyhedron

journal homepage: www.elsevier.com/locate/poly

Dual investigation of lanthanide complexes with cinnamate and phenylacetate ligands: Study of the cytotoxic properties and the catalytic oxidation of styrene

Alberto Aragón-Muriel [a], María Camprubí-Robles [b], Elena González-Rey [b], Alfonso Salinas-Castillo [c], Antonio Rodríguez-Diéguez [d], Santiago Gómez-Ruiz [e,*], Dorian Polo-Cerón [a,*]

[a] Departamento de Química, Universidad del Valle, Calle 13 No 100-00, Cali 76001000, Colombia
[b] Institute of Parasitology and Biomedicine "López-Neyra", Spanish National Research Council (CSIC), Granada E-18016, Spain
[c] ECsens, Department of Analytical Chemistry, Faculty of Sciences, University of Granada, E-18071 Granada, Spain
[d] Departamento de Química Inorgánica, Facultad de Ciencias, Universidad de Granada, E-18071 Granada, Spain
[e] Departamento de Química Inorgánica y Analítica, E.S.C.E.T., Universidad Rey Juan Carlos, E-28933 Móstoles, Madrid, Spain

ARTICLE INFO

Article history:
Received 5 December 2013
Accepted 25 February 2014
Available online 6 March 2014

Keywords:
Cytotoxicity
Toxicity
Lanthanide
Cinnamate
Phenylacetate
Styrene oxidation

ABSTRACT

Eleven lanthanide compounds [Y(cinn)$_3$] (**1**), [La(cinn)$_3$] (**2**), [La(4-OMecinn)$_3$]·2H$_2$O (**3**), [La(4-Clcinn)$_3$]·2H$_2$O (**4**), [La(4-OMephac)$_3$]·4H$_2$O (**5**), [La(4-Clphac)$_3$]·3H$_2$O (**6**), [Ce(cinn)$_3$] (**7**), [Nd(cinn)$_3$] (**8**), [Sm(cinn)$_3$]·H$_2$O (**9**), [Yb(cinn)$_3$] (**10**) and [Sm(4-OMephac)$_3$]·H$_2$O (**11**) containing carboxylato ligands (cinn = cinnamate; 4-OMecinn = 4-methoxicinnamate; Clcinn = 4-chlorocinnamate; 4-OMephac = 4-methoxyphenylacetate; 4-Clphac = 4-chlorophenylacetate) have been synthesized and characterized by elemental analysis, IR, ^{1}H and ^{13}C NMR spectroscopy, thermal analysis and X-ray diffraction powder patterns. In addition, compound **11** was characterized by single crystal X-ray diffraction studies. The cytotoxic activity of these complexes has been tested against three different human tumour cell lines HL60 (human promyelocytic leukemia), K562 (human erythromyeloblastoid leukemia) and MCF7 (breast cancer), observing a very modest cytotoxic activity for all tested compounds. In addition, toxicity tests to macrophages and erythrocytes have also been carried out, observing that none of the compounds is toxic against these immunocompetent cells. Finally, all the synthesized compounds have been tested as catalysts for styrene oxidation observing conversions higher than 50% after 19 h of reaction as well as a relatively high selectivity to two main products benzaldehyde (BzA) and 1-phenylethane-1,2-diol (PhED). Complex **7** presents the higher conversion (99.56%) with a relatively high selectivity towards PhED of 72.07%.

1. Introduction

Metal coordination complexes have shown interesting physico-chemical properties which have been exploited not only in homogeneous catalysis or in the preparation of novel materials with fascinating properties, but also in medicinal purposes as cytotoxic agents [1]. Lanthanide complexes have also attracted attention in pharmaceutical applications due to the results presented in recent research [2–6]. Especially, studies on cinnamic acid derivatives have shown anti-tumoral properties [7–12], attracting the interest of the scientists because they could be employed as potential drugs.

In addition, lanthanide complexes possess unique properties that make them attractive and promising for research, in both stoichiometric and catalytic reactions. The particular combination of their ionic radii, the Lewis acidity and the presence of unemployed 5d and 6s orbitals, provide a great advantage in coordination complexes. A remarkable variation of the ionic radius of the lanthanide series, gives the possibility of adjusting the geometrical parameters of the metal coordination sphere, optimizing the selectivity for choosing the central atom of the substrate with a radius appropriate to the specifications of the catalytic reaction [13].

Thus, another common application of lanthanide complexes may be their use as catalyst for the preparation of different compounds and/or materials. Many studies of the oxidation and epoxidation of organic substrates with lanthanide complexes have been

* Corresponding authors. Tel.: +34 914888507; fax: +34 914888143 (S. Gómez-Ruiz).
E-mail addresses: santiago.gomez@urjc.es (S. Gómez-Ruiz), dorian.polo@correounivalle.edu.co (D. Polo-Cerón).

http://dx.doi.org/10.1016/j.poly.2014.02.040
0277-5387/

reported [14–17], and for basic chemistry, the study of the oxidation of styrene is interesting because it is the simplest vinyl aromatic derivative and the catalytic studies may be the basis for further research, for example to the cosmetics industry, flavorings and pharmaceuticals [18–22].

Thus, having in mind the potential application of lanthanide complexes in biologic and catalytic processes and based on previous reports by our group on the application of metal complexes with biological activity [23,24], and catalytic properties of metal complexes [25,26], we report here the synthesis and characterization of Y(III), La(III), Ce(III), Nd(III), Sm(III) and Yb(III) complexes with *p*-substituted-cinnamate and *p*-substituted phenylacetate ligands (Fig. 1) and the toxicity against immunocompetent cells (mice macrophages and erythrocytes) and cytotoxicity against specific human cancer cells line (HL60 (human promyelocytic leukemia), K562 (human erythromyeloblastoid leukemia) and MCF7 (breast cancer). In addition, the study of the catalytic activity and selectivity of these compounds on styrene oxidation is reported.

2. Experimental

2.1. Materials and methods

trans-Cinnamic acid (cinnH), 4-methoxycinnamic acid (4-OMecinnH), 4-chlorocinnamic acid (4-ClcinnH), 4-methoxyphenylacetic acid (4-OMephacH), 4-chlorophenylacetic acid (4-ClphacH) and $LnCl_3\ xH_2O$ (Ln = Y, La, Ce, Nd, Sm, Yb) were purchased from Sigma–Aldrich and other chemicals were obtained commercially and used without further purification. The sodium cinnamates were synthesized in an equimolar reaction by the neutralization of the respective acid with NaOH solution in ethanol, the mixture was held at room temperature for 1 h with constant stirring, the solid obtained was filtered, washed with ethanol:water (1:1) and dried under vacuum. For synthesis of sodium 4-methoxyphenylacetate and sodium 4-chlorophenylacetate, the methodology described above was performed using pentane and ethyl acetate as solvents respectively. Microanalyses were carried out with a Flash EA 1112 Series CHN Analyzer. Metal concentrations were determined by EDTA titration. Infrared spectra were recorded with a NICOLET 6700 Spectrometer (4000–225 cm^{-1} with recording accuracy of 1 cm^{-1}). ^1H NMR and ^{13}C NMR spectra were recorded in DMSO-d^6 at 25 °C on a Bruker Avance II 400 spectrometer. Chemical shifts are recorded in δ values (ppm) respect to residual signals of deuterated solvents and coupling constants (J) are given in Hz. The multiplicities of carbon signals were obtained from distortionless enhancement by polarization transfer experiments (DEPT). Powder X-ray diffractograms of different samples were recorded on Panalytical X'Pert PRO X-ray diffractometer equipped with a Co Kα radiation source. The scanning range used was at least $2\theta = 5–40°$ at at 0.02° s^{-1} with a 0.25° divergence slit, 0.04 rad soller slit, 0.76 mm anti-scatter slit and a Fe filter. All scans were run at room temperature and powder patterns were generated by using X'Pert Data Collector software. TG-DTG analyses were performed with the NETZSCH STA 409 simultaneous thermal analyzer. Heating was conducted under static condition in air with a range of 298–1073 K at 10 K min^{-1}.

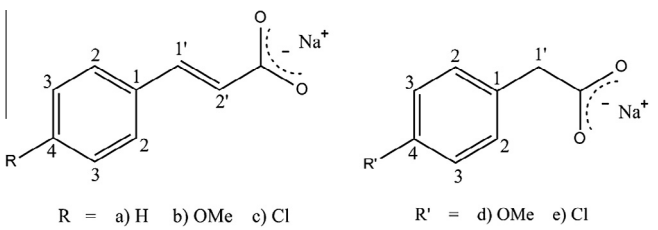

Fig. 1. The structural formula of the sodium ligand precursors (NaL): (a) sodium cinnamate Na(cinn), (b) sodium 4-methoxycinnamate Na(4-OMecinn), (c) sodium 4-chlorocinnamate Na(4-Clcinn), (d) sodium 4-methoxyphenylacetate Na(4-OMephac) and (e) sodium 4-cholorophenylacetate Na(4-Clphac).

2.2. Synthesis of lanthanide compounds

The Ln(III) complexes were prepared by using similar methods to those described in literature [27,28] (Fig. 2).

2.2.1. Synthesis of $[Y(cinn)_3]$ (**1**)

An aqueous solution (10 ml) of Na(cinn) (3 eq: 842 mg, 4.95 mmol) was slowly added to the aqueous solution (15 ml) of $YCl_3{\cdot}6H_2O$ (500 mg, 1.65 mmol) and a precipitate formed instantly. Upon the addition of the sodium salt, the solution was adjusted to pH 5 with drops of 0.1 M HCl or NaOH solution, controlled by pH-meter, then stirred for 3 h and filtered. The white precipitate was then washed with distilled water and dried in a desiccator for 2 days. Yield: 730 mg, 83 %. $C_{27}H_{21}YO_6$, Elemental analysis; C, 58.50 (calc. 61.15); H, 3.99 (3.99); Y, 16.54 (16.76)%. IR (KBr pellet cm^{-1}): 3033 w, 2924 w, 1638 s, 1597 m, 1516 s, 1451 m, sh, 1412 s, 1386 s, 1290 w, 1237 s, 1177 w, 1071 w, 987 s, 876 s, 852 w, 779 s, 749 m, 724 m, 686 s, 593 s, 554 m, 484 m. ^1H NMR (DMSO-d^6) δ (ppm) 6.51 (d, 3H, ^3J = 15.61 Hz, H-2′), 7.33 (s, 9H, H-3 and H-4 overlapped), 7.49 (d, 3H, ^3J = 16.00 Hz, H-1′), and 7.56 (d, 6H, ^3J = 2.34 Hz, H-2); ^{13}C NMR δ (ppm) 124.87 (C-2′), 128.13 (C-4), 129.24 (C-2), 129.77 (C-3), 135.64 (C-1), 136.42 (C-1′), and 176.86 (C=O). Powder XRD [d-spacings/Å (I/I°)]- 12.93 (100), 11.46 (72), 8.95 (39), 8.33 (35), 6.51 (58), 5.93 (17), 5.85 (19), 5.75 (21), 5.50 (17), 5.40 (11), 5.13 (10), 4.70 (15), 4.65 (33), 4.46 (42), 4.16 (15), 3.97 (33), 3.89 (21), 3.71 (21).

2.2.2. Synthesis of $[La(cinn)_3]$ (**2**)

The synthesis of **2** was carried out in identical manner to **1**. White powder, yield: 750 mg, 96%. $C_{27}H_{21}LaO_6$, Elemental analysis; C, 55.47 (calc. 55.88); H, 3.95 (3.65); La, 23.71 (23.93)%. IR (KBr pellet cm^{-1}): 3051 w, 1636 s, 1575 m, 1529 m, sh, 1499 s, 1450 m, 1394 s, 1289 w, 1243 s, 1200 w, 1071 w, 982 s, 879 m, 850 m, 779 s, 737 s, 688 m, 589 s, 539 m, 482 m. ^1H NMR (DMSO-d^6) δ (ppm) 6.47 (d, 3H, ^3J = 16.06 Hz, H-2′), 7.31 (s, 9H, H-3 and H-4 overlapped), 7.43 (d, 3H, ^3J = 15.81 Hz, H-1′), and 7.53 (d, 6H, ^3J = 2.76 Hz, H-2); ^{13}C NMR δ (ppm) 125.62 (C-2′), 127.51 (C-4), 128.72 (C-2), 129.07 (C-3), 135.31 (C-1), 139.89 (C-1′), and 176.62 (C=O). Powder XRD [d-spacings/Å (I/I°)]- 11.89 (100), 8.99 (6), 6.54 (29), 5.67 (28), 4.50 (9), 4.28 (22), 3.92 (10), 3.88 (4), 3.78 (5), 3.51 (5), 3.36 (4), 3.27 (6), 3.14 (8), 2.99 (8), 2.64 (4). TGA mass loss 44.00% (295–500 °C, 1 step, calc. La_2O_3 formation = 43.86 %).

2.2.3. Synthesis of $[La(4\text{-}OMecinn)_3]{\cdot}2H_2O$ (**3**)

The synthesis of **3** was carried out in identical manner to **1**. White powder, yield: 800 mg, 84%. $C_{30}H_{31}LaO_{11}$, Elemental analysis; C, 49.81 (calc. 51.00); H, 4.37 (4.42); La, 19.79 (19.66)%. IR (KBr pellet cm^{-1}): 3342 m, br, 2935 w, 2837 w, 1638 s, 1606 s, 1573 w, 1513 s, 1426 s, 1404 s, 1305 m, 1246 s, 1174 s, 1109 m, 1032 s, 985 s, 879 m, 832 s, 781 m, 722 m, 558 m, 519 w, 268 s, 238 s. ^1H NMR (DMSO-d^6) δ (ppm) 3.73 (s, 9H, –O–CH_3), 6.35 (d, 3H, ^3J = 15.65 Hz, H-2′), 6.83 (d, 6H, ^3J = 7.34 Hz, H-3), 7.41 (d, 3H, ^3J = 16.14 Hz, H-1′), and 7.45 (d, 6H, ^3J = 8.31 Hz, H-2); ^{13}C NMR δ (ppm) 55.65 (–O–CH_3), 114.64 (C-3), 123.40 (C-2′), 128.36 (C-1), 129.62 (C-2), 140.50 (C-1'), 160.55(C-4), and 177.30 (C=O). Powder XRD [d-spacings/Å (I/I°)]- 24.21 (100), 9.36 (14), 8.49 (4), 7.61 (19), 7.24 (17), 7.02 (64), 5.89 (7), 5.53 (9), 4.66 (13), 4.44 (4), 4.29 (4), 4.04 (5), 3.80 (5). TGA mass loss 4.89% (70–120 °C, 1