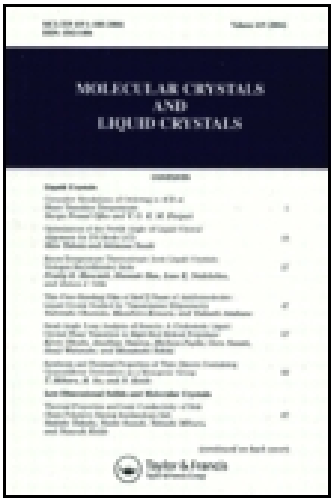

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Liquid Crystalline Cholesterol-Based *Ortho*-Palladated Curcumin Complexes as Multifunctional Biomaterials

Daniela Pucci[1], Rossana Bloise[1], Anna Bellusci[1], Sergio Bernardini[2], Mauro Ghedini[1], Alessandra Valentini[2], and Alessandra Crispini[1]
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Mononuclear ortho-*palladated complexes containing 2-phenylquinoline ligand functionalized with a chiral entity and a biologically active O,O chelated ligand have been synthesized and fully characterized. The evaluation of the liquid crystalline properties of these non-conventional compounds is reported in view of a potential use of these organometallic systems in generating new bifunctional biomaterials.*

Keywords: chirality; curcumin; cyclopalladated 2-phenylquinoline complexes; tropolone

INTRODUCTION

Despite of the fact that thousands of metal-complexes have been produced since the discovery of the anticancer activity of *cis*-platin and its analogues, there is a growing involvement on the design of new coordination compounds that will combat intrinsic and acquired drug resistance and that will reduce the toxic side effects of the chemioterapy. In particular, the success of organo-transition metal compounds in combating cancer has increased the interest in the synthesis of pharmaceuticals based on organometallic compounds. Cyclopalladated

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complexes are promising antitumor drugs effective both *in vitro* and *in vivo*, when compared to many platinum-based anticancer compounds [1].

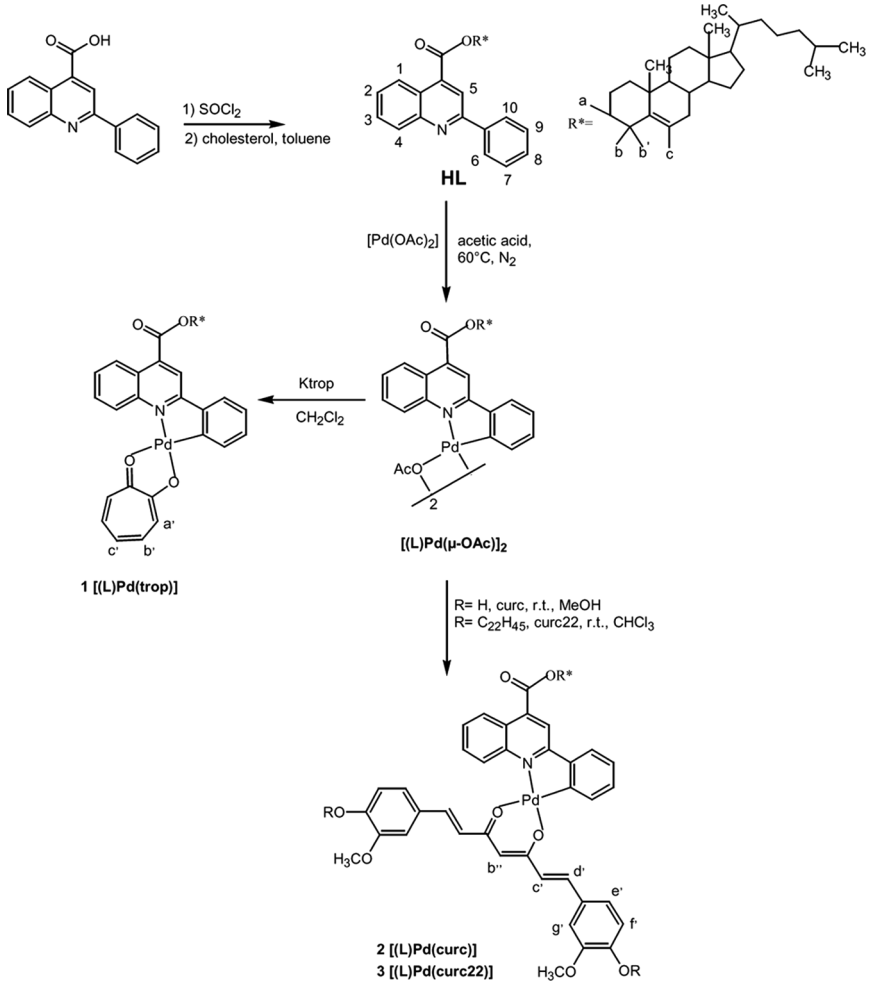
Our experience in cyclopalladation in the field of liquid crystals [2] and most recently in *ortho*-palladation to produce antitumor agents [3,4] encouraged the design of a new cyclometallating ligand, based on the bioactive 2-phenylquinoline framework on which a cholesteryl ester unit has been introduced as chiral terminal substituent. The promesogenic cholesterol unit has been choosen for its universal affinity for cell membranes, the ability to self order into liquid crystalline state and because its use into liposomes has been shown to reduce significantly leakage of the encapsulated drug during circulation in the extracellular moiety [5]. In particular we have investigated the cyclopalladating ability of this ligand by synthetizing the corresponding dinuclear cyclopalladated complex which is the first step towards the design of hybrid species, combining in a single molecule two bioactive chelated functional moieties. Indeed, the 2-phenylquinoline cyclopalladated fragment has been conjugated to a ligand of established effectiveness in combating cancer, the curcumin (1,7-bis(4-hydroxy-3-methoxyphenyl)-1,6- heptadiene-3,5-dione, diferuloyl methane), curc, and to a newly synthetized alkoxy curcumin derivative, in which a long alkyl chain has been grafted onto the 4 position of the aromatic ring, curc22. We envisaged the possibility of using such systems to design amphiphilic metallomesogens in order to get multifunctional biomaterials bearing at the same time the active principe and the delivery component, becoming innovative tools in establishing new and effective therapies.

Herein we report the synthesis and the thermal characterization of the new functionalized 2-phenylquinoline ligand **HL** obtained introducing a cholesteryl ester unit as chiral chain, and of a series of derivatives containing O,O chelating bioactive ligands (O,O = monoanionic form of tropolone, curcumin and its newly synthetized alkoxy derivative, curc22), of general formula **[(L)Pd(O,O)]** (Scheme 1). The thermal behaviour of the obtained complexes has been investigated revealing the formation of liquid crystals with different mesophase organizations depending on the shape of the molecule. Moreover, we have performed also preliminary biological studies on the same cancer cell line tested on the analogous curcumin derivatives [4] and the results are herein reported.

EXPERIMENTAL SECTION

Measurements

The ^{1}H NMR spectra were recorded on a Bruker Avance AC-300 spectrometer in $CDCl_3$ solution, using tetramethylsilane (TMS) as



SCHEME 1 Synthetic route to **HL** and the corrisponding **[(L)Pd(O,O)]** complexes.

internal standard. Elemental analyses (CHN) were performed with a Perkin Elmer 2400 microanalyzer by the Microanalytical Laboratory at the University of Calabria. Infrared spectra (KBr) were recorded on a Perkin Elmer Spectrum One spectrometer. The textures of the mesophases were studied with a Leica DMLP polarizing microscope equipped with a CaLCTec heating stage. The transition temperatures were measured on a Perkin Elmer DSC 7 Differential Scanning Calorimeter with a heating and cooling rate of 10°C/min. The instrument was calibrated with Indium.

Synthesis

2-Phenyl-4-quinoline-carboxylic acid was purchased from Aldrich and used without purification, while the curcumin, purchased from Aldrich, was used after separation into individual components as previously reported [4]. Curc22 compound was prepared as described in the literature [4]. The potassium tropolonato salt was prepared stirring the tropolone in a basic solution of EtOH with a stoichiometric rate of KOH.

Synthesis of Cholesteryl-2-phenylquinoline-4-carboxylate, HL

To 2-phenyl-4-quinoline carboxilic acid (2 g, 8.02 mmol), under nitrogen atmosphere, was added $SOCl_2$ (10 mL) and the mixture was stirred at 80°C for 24 h. The solvent and the excess of $SOCl_2$ were removed under vacuum and the chloride of the 2-phenyl-4-quinoline carboxilic acid (2.10 g, 8.02 mmol) was immediately reacted with a solution of cholesterol (3.71 g, 9.6 mmol) in 50 mL of toluene. The mixture was stirred at 0°C, under nitrogen atmosphere, over a period of 30 min and then at 110°C for 48 h. The solvent was removed under vacuum and the remaining residue was extracted with a basic solution of $NaHCO_3$. After crystallization from methanol (−20°C), the pure white solid **L** was obtained. Yield: 85%. Anal. Calcd for $C_{43}H_{55}NO_2$ (Mw = 617.91): C 83.58 H 8.97 N 2.26. Found C 83.07 H 9.23 N 2.66%. ^{1}H-NMR (300 MHz, $CDCl_3$): δ 8.71 (d, $J = 7.59$ Hz, H_1), 8.35 (s, H_5), 8.21 (m, 3H, $H_{6,10,4}$), 7.76 (t, $J = 5.47$ Hz, H_3), 7.62 (t, $J = 5.57$ Hz, H_2), 7.53 (m, 3H, $H_{7,\ 8,\ 9}$), 5.48 (d, $J = 3.9$ Hz, H_c), 5.05 (m, 1H, H_a), 2.58 (d, 2H, $J = 7.81$ Hz, $H_{b,b'}$), 0.70–2.09 (m, 41H, C−H). IR (KBr, ν/cm^{-1}): 2941-2866 (C−H), 1713 (C−OOR).

Synthesis of [(L)Pd(μ-OAc)]$_2$

To a solution of **HL** (0.5 g, 0.809 mmol) in 15 mL of acetic acid was added palladium (II) acetato (0.181 g, 0.809 mmol) at 60°C, under nitrogen atmosphere, and immediatly a red precipitate was obtained. The resulting suspension was stirred over a period of 12 h. The product was filtered, washed with EtOH and recrystallized from MeOH (−20°C). Yield: 90%. Anal. Calcd for $C_{90}H_{114}O_8N_2Pd_2$ (Mw = 1564.85): C 69.07 H 7.34 N 1.79. Found C 69.12 H 7.75 N 1.89%. ^{1}H-NMR (300 MHz, $CDCl_3$): δ 8.54 (d, $J = 6.71$ Hz, 2H, H_{1trans}), 8.49 (d, 2H, H_{1cis}), 8.24 (d, $J = 7.33$ Hz, 2H, H_{7trans}), 8.12 (d,2H, H_{7cis}), 7.71 (s, 2H, H_{5trans}), 7.50 (m, 2H, H_{8trans}), 7.42 (m, 2H, H_{9trans}), 7.18 (m, 2H, H_{8cis}), 7.08 (m, 2H, H_{9cis}), 6.85 (d, $J = 7.94$ Hz, 2H, H_{4cis}), 6.80 (d, 2H, H_{4trans}), 6.70 (m, 4H, $H_{3,10cis}$), 6.62 (t, 2H, H_{2cis}), 6.53

(m, 2H, H_{3trans}) 6.46 (t, $J = 5.49$ Hz, 2H, $H_{10trans}$), 6.22 (m, 2H, H_{2trans}), 5.54 (d, $J = 7.32$ Hz, $H_{c\ trans}$), 5.49 (d, 2H, $H_{c\ cis}$), 5.09 (m, 2H, $H_{a\ trans}$), 5.02 (m, 2H, H_{acis}), 2.66 (d, 2H, $J = 10.6$ Hz, $H_{b,b'trans}$), 2.60 (d, 2H, $H_{b,b'cis}$), 0.70–2.39 (m, 41H, C–H). IR (KBr, ν/cm^{-1}): 2934-2865 (C–H), 1726 (C–O), 1570 (C–O acetato).

Synthesis of [(L)Pd(trop)], 1

Ktrop (0.030 g, 0.191 mmol), was added to a solution of [(L)Pd(μ-OAc)]$_2$, **1** (0.15 g, 0.095 mmol), in 15 mL of CH_2Cl_2. The resulting red solution that was stirred for 4 days at room temperature, became yellow. This solution was filtered, concentrate evaporating the solvent and recrystallized from EtOH (−20°C). Yield 85%. Anal. Calcd for $C_{50}H_{60}O_4NPd$ (Mw = 845.44): C 71.03 H 7.15 N 1.65. Found C 71.25 H 6.98 N 1.51%. ^{1}H-NMR (300 MHz $CDCl_3$): δ 9.47 (d, $J = 8.48$ Hz, H_1), 8.65 (d, 1H, $J = 7.36$ Hz, H_4), 8.17 (s, 1H, H_5), 7.87 (t, 1H, $J = 5.52$, H_8), 7.75 (d, 1H, $J = 8.93$ Hz, H_{10}) 7.63 (t, 1H, $J = 7.25$ Hz H_9), 7.56 (d, 1H, $J = 9.14$ Hz, H_7) 7.39 (m, 4H, $H_{a',a'',b',b''}$), 7.20 (m, 2H, $H_{2,3}$), 6.93 (m, 1H,$H_{c'}$), 5.50 (d, $J = 3.9$ Hz, H_c), 5.05 (m, 1H, H_a), 2.58 (d, 2H, $J = 7.80$ Hz, $H_{b,b'}$), 0.69–2.13 (m, 41H, C–H). IR (KBr, ν/cm^{-1}): 2945-2865 (C–H), 1721 (C–O), 1592 (C–C trop).

Synthesis of [(L)Pd(curc)], 2

A suspension of [(L)Pd(μ-OAc)]$_2$, **1** (0.15 g, 0.095 mmol) in 10 mL of MeOH was reacted with a solution of pure curcumin (0.070 g, 0.191 mmol) in 10 mL of MeOH. The resulting red mixture, that became yellow, was stirred at room temperature for 48 h. The yellow solid was filtered and recrystallized from MeOH. Yield 70%. Anal. Calcd for $C_{64}H_{74}O_8NPd + 2\ H_2O$ (Mw = 1127.74): C 68.16 H 6.97 N 1.24. Found C 68.61 H 6.89 N 1.52%. ^{1}H-NMR (300 MHz $CDCl_3$): δ 9.67 (d, 1H, $J = 8{,}54$ Hz, H_1), 8.65 (d, 1H, $J = 8.55$ Hz, H_4), 8.22 (s, 1H, H_5), 7.85 (m, 2H, $H_{8,9}$), 7.60 (m, 4H, $H_{3,7,d',d''}$), 7.25 (m, 2H, $H_{2,10}$), 7.10 (m, 4H, $H_{e',e'',g',g''}$), 6.93 (d, 2H, $J = 8.85$ Hz, $H_{f'f''}$), 6.60 (d, 2H, $J = 15.56$ Hz, $H_{c'c''}$), 5.79 (s, 2H, OHcurc), 5.72 (s, 1H, $H_{b'}$), 5.49 (d, $J =$ 3.9 Hz, H_c), 5.05 (m, 1H, H_a), 3.95 (s, 6H, OCH_3), 2.60 (d, 2H, $J = 7.80$ Hz, $H_{b,b'}$), 0.70–2.25 (m, 41H, C–H). IR (KBr, ν/cm^{-1}): 1): 2948 (C–H), 1721 (C–O), 1626 (C–Ocurc), 1508 (C–C).

Synthesis of [(L)Pd(curc22)], 3

To a solution of curc22 (0.063 g, 0.063 mmol) in 15 mL of $CHCl_3$ was added the binuclear precursor [(L)Pd(μ-OAc)]$_2$, **1** (0.050 g, 0.031 mmol).

The resulting orange solution was stirred for 3 days at room temperature. The yellow solid that was obtained was filtered and recrystallized from EtO_2. Yield: 75%. Anal. Calcd for $C_{108}H_{161}O_8NPd + 3H_2O$ (Mw = 1761.90): C 73.62 H 9.55 N 0.79. Found C 73.66 H 9.65 N 0.95%. ^{1}H−NMR (300 MHz $CDCl_3$): δ 9.67 (d, 1H, $J = 9.00$ Hz, H_1), 8.66 (d, 1H, $J = 9.00$ Hz, H_4), 8.27 (s, 1H, H_5), 7.88 (m, 2H, $H_{8,9}$), 7.64 (m, 4H, $H_{3,7,d',d''}$), 7.25 (m, 2H, $H_{2,10}$), 7.13 (m, 4H, $H_{g',g'',e',e''}$), 6.99 (d, 2H, $J = 7{,}70$ Hz, $H_{f',f''}$), 6.65 (d, 2H, $J = 15.11$ Hz, $H_{c',c''}$), 5.75 (s, 1H, H_b), 5.50 (d, $J = 3.9$ Hz, H_c), 5.05 (m, 1H, H_a), 4.05 (d, 4H, $OCH_2(CH_2)_{20}CH_3$), 3.93 (s, 6H, OCH_3curc), 2.59 (d, 2H, $J = 7.80$ Hz, $H_{b,b'}$), 0.70–2.01 (m, 41H, C-H). IR (KBr, ν/cm^{-1}): 2850–2918 (C−H), 1721 (C−O), 1625 (C–Ocurc22), 1510 (C−C).

Cell Lines and Cytotoxic Assay Performed on Complex 2

DU145 human prostrate cancer cell line was grown in RPMI-1640 (Gibco) supplemented with 10% of fetal bovine serum (GIBCO), 5% of L-glutamine (GIBCO) and antibiotics, under standard conditions (37°C temperature, 5% CO_2 in a humidified atmosphere).

For cytotoxic assays, cells were plated in 96-well plates (Falcon, CA) in 100 uL of culture medium. All species were dissolved in DMSO. For each experiment drugs were serially diluted in cell culture medium to the desired concentrations and an equal volume of the diluted solution (100 uL/well) was added to the cells. DMSO was administered as control. Each treatment was performed in triplicate in three indipendent experiments. Cells were continuously exposed to the curcuminoid derivative **2** for 72 h. In order to determine the cytotoxic effect at the end of drug incubation, MTS solution (3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(4-sulfophenyl)-2H-tetrazolium, inner salt, Promega, 20 uL/well) was added to the cells. The plates were incubated for 2 h at 37°C and then the absorbance at 490 nm was measured using Sirio-S (SEAC, Radim Group). Results are expressed as mean ± standard deviation (SD) of the percentage of viable cells at each drug concentration compared to the untreated cells.

RESULTS AND DISCUSSION

Synthesis

The cyclopalladating ligand **HL** has been obtained through a two step reaction: 2-phenyl-4-quinoline carboxylic acid reacts with thionyl chloride to give rise to the corresponding acid chloride whose esterification with cholesterol, in toluene, affords **HL** in 85% yield.

The synthetic pathway used to obtain the [(L)Pd(O,O)] complexes **1–3** is illustrated in Scheme 1.

In order to reach the target mononuclear cyclopalladated derivatives we treated **HL** with palladium(II) acetato, in glacial acetic acid solution, forming the pure acetato-bridged dimeric product, **[(L)Pd(μ-OAc)]$_2$**, which was obtained in a 90% yield. The IR spectrum of **[(L)Pd(μ-OAc)]$_2$** revealed the presence of two bands, at 1565 and 1411 cm^{-1}, assigned to the asymmetric and symmetric stretching modes of the acetato group, confirming the formation of the bridged acetato derivative. Moreover, a shift of the $\nu_{C=O}$ band from 1717 cm^{-1} to 1727 cm^{-1} with respect to **HL**, is observed. The ^{1}H NMR spectrum of **[(L)Pd(μ-OAc)]$_2$** revealed the absence of the H^6 proton, proving the formation of the bridged acetato derivative. In this spectrum it was also observed the presence of two isomers. According to the literature data about of similar dimeric acetato species [6,7], we popose that the higher signals proportion can be assigned to the *trans* isomer (5:1).

The **[(L)Pd(μ-OAc)]$_2$** complex is a good starting material for the synthesis of the corresponding mononuclear *ortho*-palladated derivatives **1-3** since the OAc anion is the appropriate leaving group to encourage the chelation of the reacted O,O incoming ligands (Experimental Section). All complexes have been fully characterized by ^{1}H NMR, FT-IR and elemental analysis, proving the expected [(L)Pd(O,O)]stoichiometry.

Thermal Behaviour

Although the ligand **HL** is not liquid crystal, the complexation to the palladium gave rise to the new liquid crystalline cyclopalladated complexes,which all showed thermally reproducible mesomorphism, which was evidenced by a combination of optical microscopy (POM), differential scanning calorimetry (DSC) and powder X-ray diffraction analysis at variable temperature (PXRD). Thermal data are summarized in Table 1.

The identification of the mesophases was firstly performed by observation of the optical textures: an oily streaks texture, for **[(L)Pd(μ-OAc)]$_2$**; a very fine schlieren texture for **[(L)Pd(trop)]**, **1**, and **[(L)Pd(curc)]**, **2**. The texture of **[(L)Pd(curc22)]**, **3**, showed Maltese crosses suggesting the existence of columnar mesomorphism. X-ray diffraction at variable temperature were carried out to confirm the nature of the mesophases.

The PXRD recorded at 240°C of the dinuclear **[(L)Pd(μ-OAc)]$_2$** derivative has revealed the presence of a chiral smectic phase through

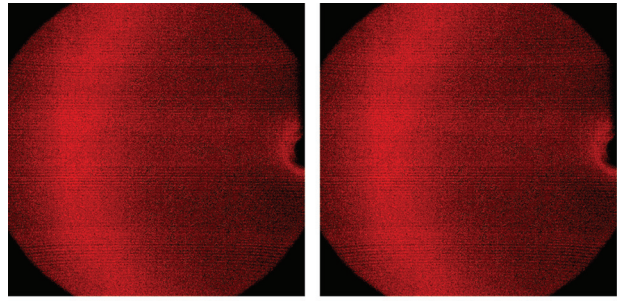
TABLE 1 Thermal Properties of Complexes **1–3**

Complexes	Phases[a]	Transition temperatures (°C)	ΔH/kJ mol^{-1}
[(L)Pd(μ-OAc)]$_2$	C-Smc*	195.6	24.93
	Smc*-I	225.5	6.32
[(L)Pd(trop)] **1**	C-Ch	135[a]	
	Ch-I	270[a]	
[(L)Pd(curc)] **2**	C-Col$_{rect}$	140	3.67
	Col$_{rect}$-I$_{dec}$	220.1	
[(L)Pd(curc22)] **3**	C-C′	53	5.61
	C′-Col$_{hex}$	65.2	23.88
	Col$_{hex}$-I	200[b]	

[a]Cr: Crystal; Ch: Cholestric; Col: Columnar; I: Isotropic liquid
[b]optical data

the presence of a quite broad peak in the small angle region centred at 49.5 Å (Fig. 1a). The variation in the shape of the molecule, with the introduction of the tropolone ligand causes the loss of the lamellar order and in the case of **[(L)Pd(trop)]**, **1**, a more disordered molecular arrangement is found. The PXRD in this case is characterized by a broad peak at $2\theta \approx 20$ deg, which is typical of a cholesteric structure (Fig. 1b) [8].

Replacement of the tropolonate unit by the curcuminoid co-ligands allows a peculiar combination of two different molecular architectures. The rather rod-like pheylquinoline unit with an half-disc-shaped diketonate moiety gives rise to an unusual molecular shape which deeply influences the mesophase type. Indeed a discotic mesomorphism is found for both curcuminoid derivatives **2** and **3**.



(a) (b)

FIGURE 1 X ray diffraction patterns of nonaligned samples of the (a) smectic chiral phase of **[(L)Pd(μ-OAc)]$_2$** and (b) cholesteric phase of **1**.

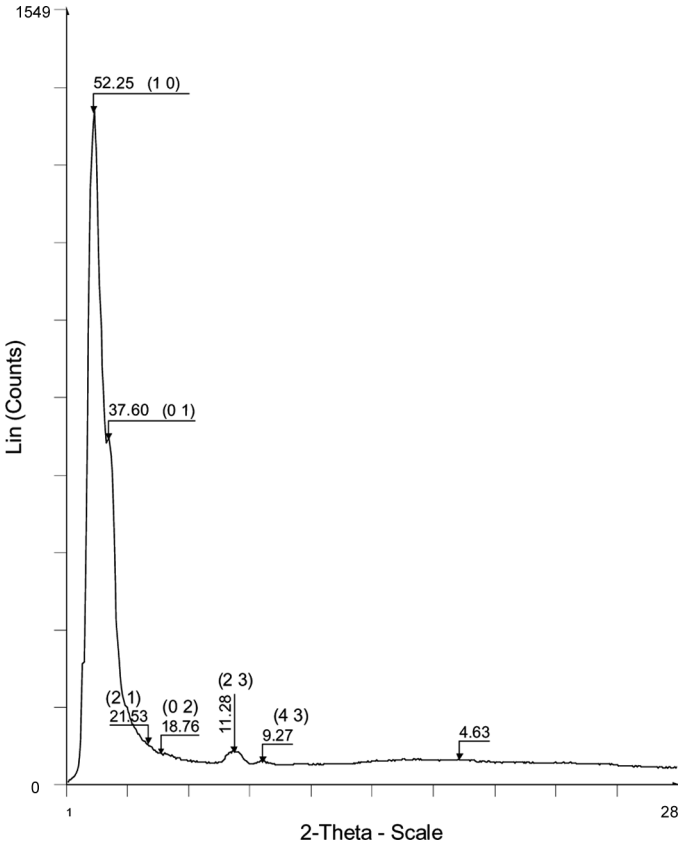


FIGURE 2 X ray diffraction pattern of a non aligned sample of **2**, recorded at 180°C on cooling.

The XRD pattern of **2** recorded at 180°C on cooling revealed a rectangular columnar mesophase, characterized by two sharp fundamental peaks in the low angle region (Fig. 2). The strong low angle peaks are indexed as (10) and (01), leading to the indexation of the peaks in the middle angle region [calculated d (Å) values for (21), 21.5, (02), 18.8, (23), 11.3, (43), 9.1] and to the calculated lattice parameters $a = 52.3$ Å and $b = 37.6$ Å.

By adding two alphatic chains to the curcumin, a transition from rectangular to hexagonal columnar symmetry organization is found. The XRD pattern of complex **3** is typical of a two-dimensional hexagonal lattice with a cell parameter a of 44.7Å. In the wide angle region a broad halo centred at 4.6 Å and corresponding to the liquid-like correlations between side chains, is observed.

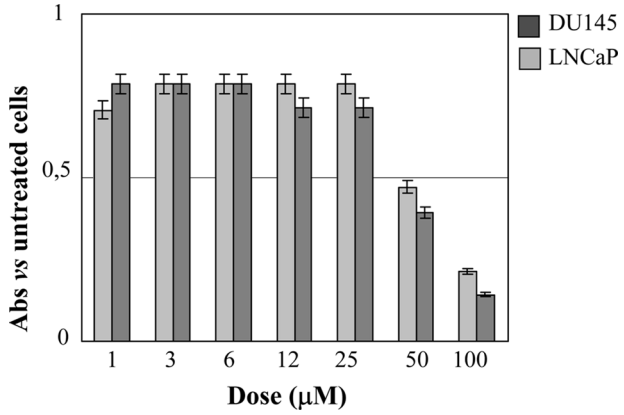


FIGURE 3 Cytotoxic activity of **[(L)Pd(curc)]**, **2**, towards DU145 and LNCaP human prostate cancer cells.

We have investigated the cytotoxic effect of the more soluble mononuclear complex, **[(L)Pd(curc)] 2**, against the androgen-unsensitive (DU145) cell line, previously tested on analogous curcumin derivatives [4], and also against an androgen-sensitive (LNCaP) human prostate cancer cell line in order to study the influence of the cholesteryl fragment on the overall framework. Cell viability was assessed after 72 hours of continuous exposure to compound **2**, using a colorimetric assay (MTS). The cytotoxic activity of **curc** was assessed under identical conditions and used as reference for the activity of the corresponding complex.

Complex **[(L)Pd(curc)]**, **2**, induces of about 55% of cell growth inhibition in both cell lines, at 50 μM dose, suggesting that the combination of two different molecular sub-units around a metal centre enhances the cytotoxicity compared to curcumin and confirms the useful approach in the synthesis of heteroleptic systems (Fig. 3).

CONCLUSIONS

The 2-phenylquinoline ligand has been functionalised with a chiral terminal substituent, the cholesteryl ester unit, and cyclopalladated producing a new dinuclear bridged acetato derivative in high yields. The corresponding heteroligand mononuclear complexes **[LPd(O,O)]** have been synthesizedby conjugating the cyclopalladated fragment with O,O chelating bioactive ligands such as tropolone and cucuminoid β-diketones. Despite of the ligand shows no mesomorphism, the

coordination to the palladium(II) has led to metallomesogenic species for which a transition from calamitic to columnar organisation of the molecules is observed. This transition strongly depends on the overall molecular shape as the geometrical features of the rather calamitic dinuclear roof-shaped acetato-bridged complex and of the mononuclear tropolonate derivative lead to a more or less parallel organization of the molecules which is favorable for disordered calamitic chiral mesophases. The replacement of the tropolonate unit with the curcuminoid co-ligands leads to the calamitic/discotic cross-over point due to the peculiar combination of two different molecular architectures: the rather rod-like pheylquinoline unit and an half-disc-shaped diketonate moiety. The resulting unusual molecular shape of the curcumin derivatives deeply influences the molecular organization within the mesophase, inducing the formation of columnar mesomorphism in the case of **[LPd(curc)]**, **2**, complex. A transition from rectangular to hexagonal columnar symmetry organization in **[LPd(curc22)]**, **3** is due to the introduction of long flexible substituents into the curcumin fragment.

A promising biological activity based on the preliminary *in vitro* anticancer screening against two human prostatic cancer cell lines has been found for **[(L)Pd(curc)]**, **2**. These results prompt us to think that, through the careful choice of the molecular building blocks, cyclopalladated mesogens can produce, more than purely organic species: i) molecular shapes easily modulated; ii) multifunctional biomaterials bearing at the same time the active principal and the delivery component, becoming innovative tool in establishing new and effective anticancer therapies.

Finally, it is noteworthy that the properties exhibited by the present complexes suggest that metallomesogens can be conveniently considered for applications requiring bioactive molecules.

REFERENCES

[1] (a) Allardyce, C. S., Dorcier, A., Scolaro, C., & Dyson. P. J. (2005). *Appl. Organomet. Chem.*, *19*, 1; (b) Dupont, J., Consorti, C. S., & Spencer. J. (2005). *Chem. Rev.*, *105*, 2527.

[2] Ghedini, M., Aiello, I., Crispini, A., Golemme, A., La Deda, M., & Pucci, D. (2006). *Coord. Chem. Rev.*, *250*, 1373.

[3] Pucci, D., Albertini, V., Bloise, R., Bellusci, A., Cataldi, A., Catapano, C. V., Ghedini, M., & Crispini. A. (2006). *J. Inorg. Biochem.*, *100*, 1575.

[4] Pucci, D., Bloise, R., Bellusci, A., Bernardini, S., Ghedini, M., Pirillo, S., Valentini, A., & Crispini. A. (2007). *J. Inorg. Biochem.*, *101*, 1013.

[5] Simoes, S., Moreira, J. N., Fonseca, C., Duzgunes, N., & Lima. M. C. P. (2004). *Adv. Drug Del. Rev.*, *56*, 947.

[6] Espinet, P., Lalinde, E., Marcos, M., Perez, J., & Serrano, J. L. (1990). *Organometallics*, *9*, 555.
[7] Lehmann, M., Marcos, M., Serrano, J. L., & Sierra, T. (2001). *Chem. Mater.*, *13*, 4374.
[8] Zhang, B.-Y., Hu, J.-S., Jia, Y.-G., & Du, B.-G. (2003). *Macromol. Chem. Phys.*, *204*, 2123.