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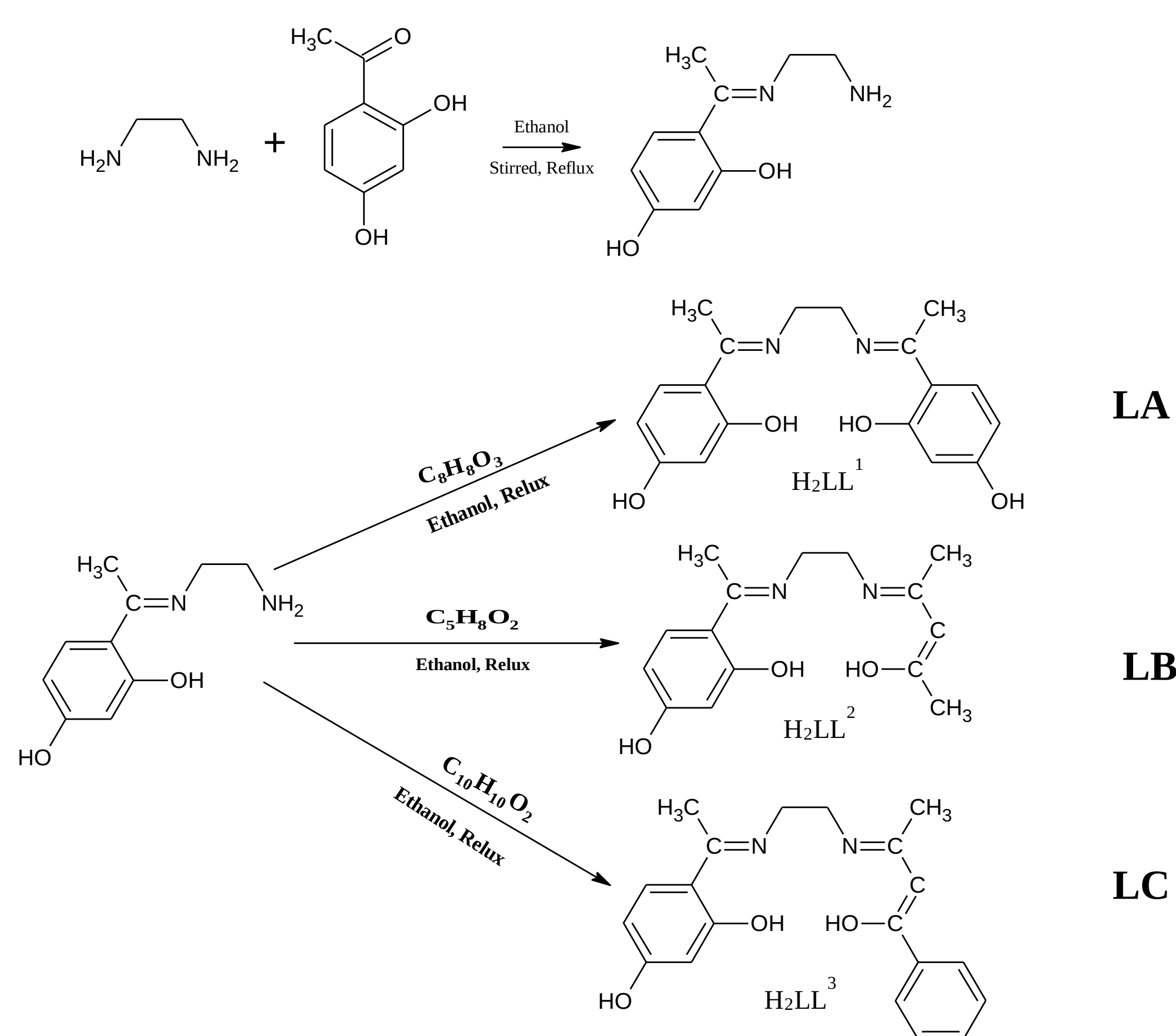
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INTRODUCTION

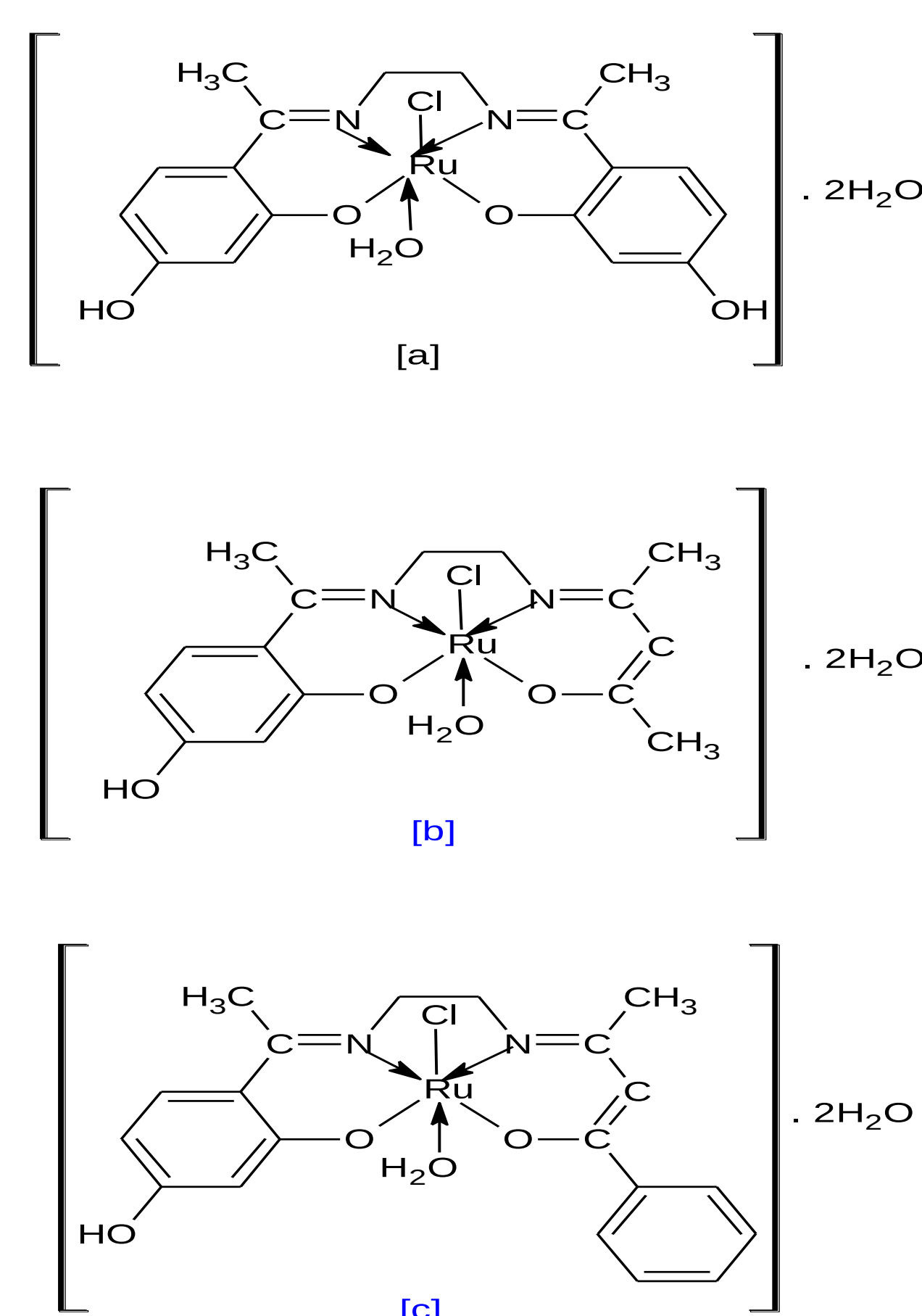
Schiff bases are an important class of compounds widely used in the medicinal and pharmaceutical fields. Schiff bases of biologically important benzophenone based and its derivatives are used as sunscreens for humans [1-2]. Tetradentate Schiff bases used in recent times in the development of single-site polymerization catalysts based on non-cyclopentadienyl complexes [2]. Metal complexes containing Schiff base are of interest because of their electronic properties that can be modified by suitable functionalization with amine and cyclic substituents [1-2]. Schiff base-transition metal complexes are known to be one of the most modifiable and comprehensively studied systems with applications in clinical and analytical fields. Metal-based antioxidants have gained recent attention for their ability to protect living organisms and cells from damage caused by oxidative stress or scavenge free radicals [2-5]. Reactive oxygen species (ROS) or free radicals are products of the *in vivo* physiological and biochemical processes in the living cells [1] that could cause lipid peroxidation and may lead to diseases such as cancer, cardiovascular diseases, immunodeficiency, liver injury, and other infections [1,5]. In order to safeguard the human body against cell damage by oxidative species, an antioxidant is of paramount importance [5]. In view of growing interest in oxygenations and azomethination of Ru(III) complexes for the development of new therapeutic agents and DNA probes for disease defence, we report in the present communication the synthesis and characterization of some stable Ru(III) Schiff bases complexes of the type [RuCl(LL')(H₂O)].2H₂O (LL' = LA, LB, LC).

MATERIALS AND METHODS

Reaction route for the preparation of the Schiff base ligands (LA- LC)



Proposed structure of Schiff bases Ru(III) complexes



RESULTS AND DISCUSSION

Mononuclear ruthenium(III) complexes of the type [RuCl(LL')(H₂O)] (LL' = LA, LB, LC) (LL' = dibasic tetradentate Schiff base ligands) were synthesized in good yields from the reactions of RuCl₃·3H₂O with Schiff base ligands in 1:1 molar ratio in Absolute EtOH to give hexa-coordinated ruthenium(III) Schiff base complexes as shown in the representation below:



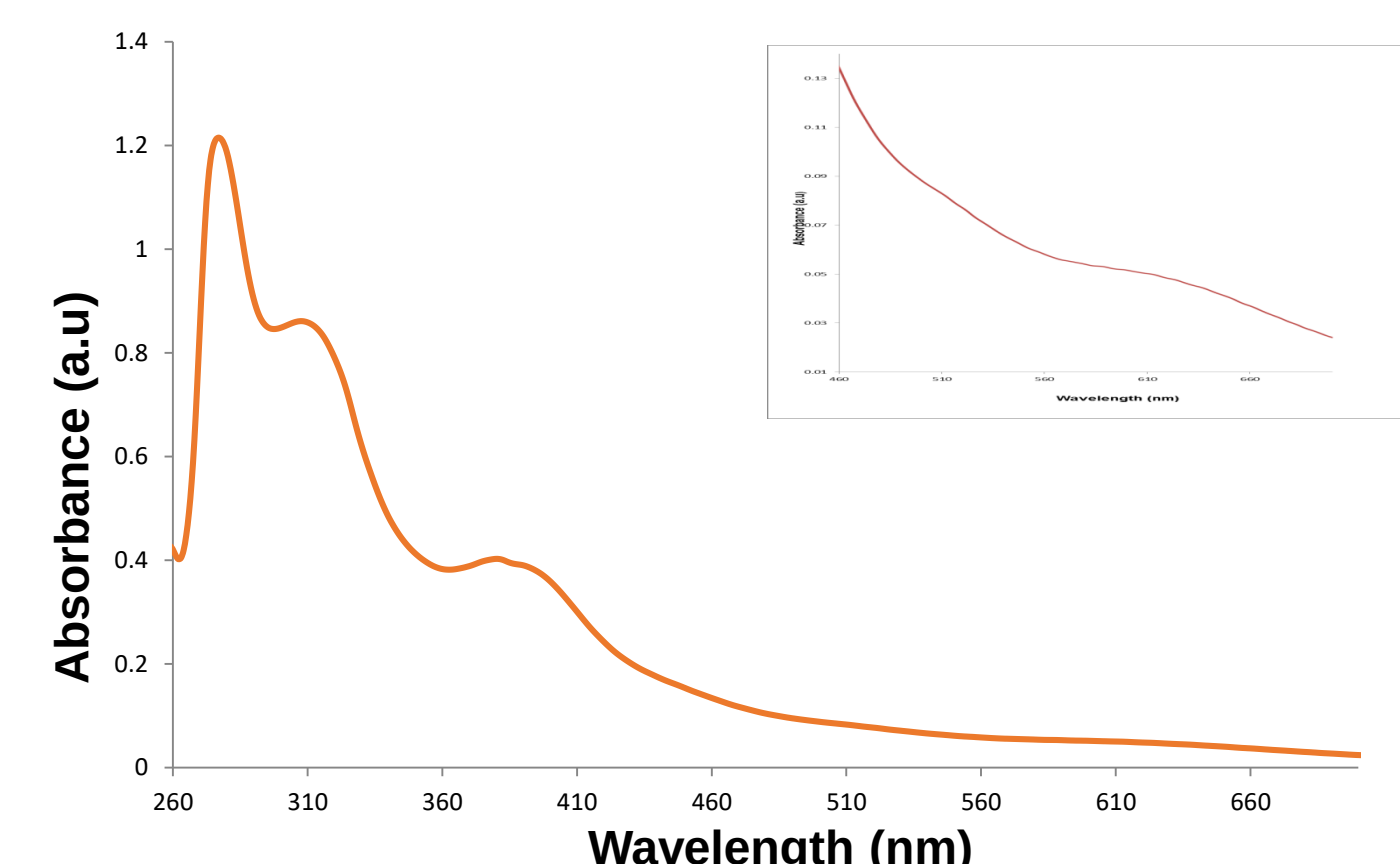
Where H₂LL = LA = [OHC₆H₃OHC(CH₃):N(C₂H₄)N:C(CH₃)HOC₆H₃OH]; LB = [OHC₆H₃OHC(CH₃):N(C₂H₄)N:C(CH₃)CH:C(CH₃)OH], and LC = [OHC₆H₃OHC(CH₃):N(C₂H₄)N:C(CH₃)CH:C(C₆H₅)OH]. The synthesized mononuclear ruthenium(III) Schiff base complexes are stable in air at room temperature, non-hygroscopic in nature and highly soluble in common solvents such as dichloromethane, acetonitrile, chloroform, DMF and DMSO producing intense colour in their solutions.

Infrared spectra

The IR spectra of the free ligands showed bands in the region 3475-3479, 2873-3076, 1605-1616, 1470-1588 and 1171-1288 cm⁻¹ assignable to ν(OH), ν(CH₃/CH₂), ν(C=N), ν(C=C), ν(C-O) respectively [2-5]. The free Schiff base ligands (LA, LB, LC) showed a very strong absorption in the 1605-1616 cm⁻¹ range in their IR spectra which are characteristic of the azomethine ν(C=N) group.

Electronic spectra

The electronic spectra of ruthenium(III) complexes were recorded in DMF in the range 900–200 nm. The complexes showed three to four bands in the region 650–280 nm. Ruthenium(III) ground state is ²T_{2g} and the first excited doublet levels in the order of increasing energy are ²A_{2g} and ²T_{1g}, which arise from t_{2g}⁴e_g¹ configuration. In general the electronic spectra of all the complexes are characteristic of an octahedral environment around ruthenium(III) ions [2].

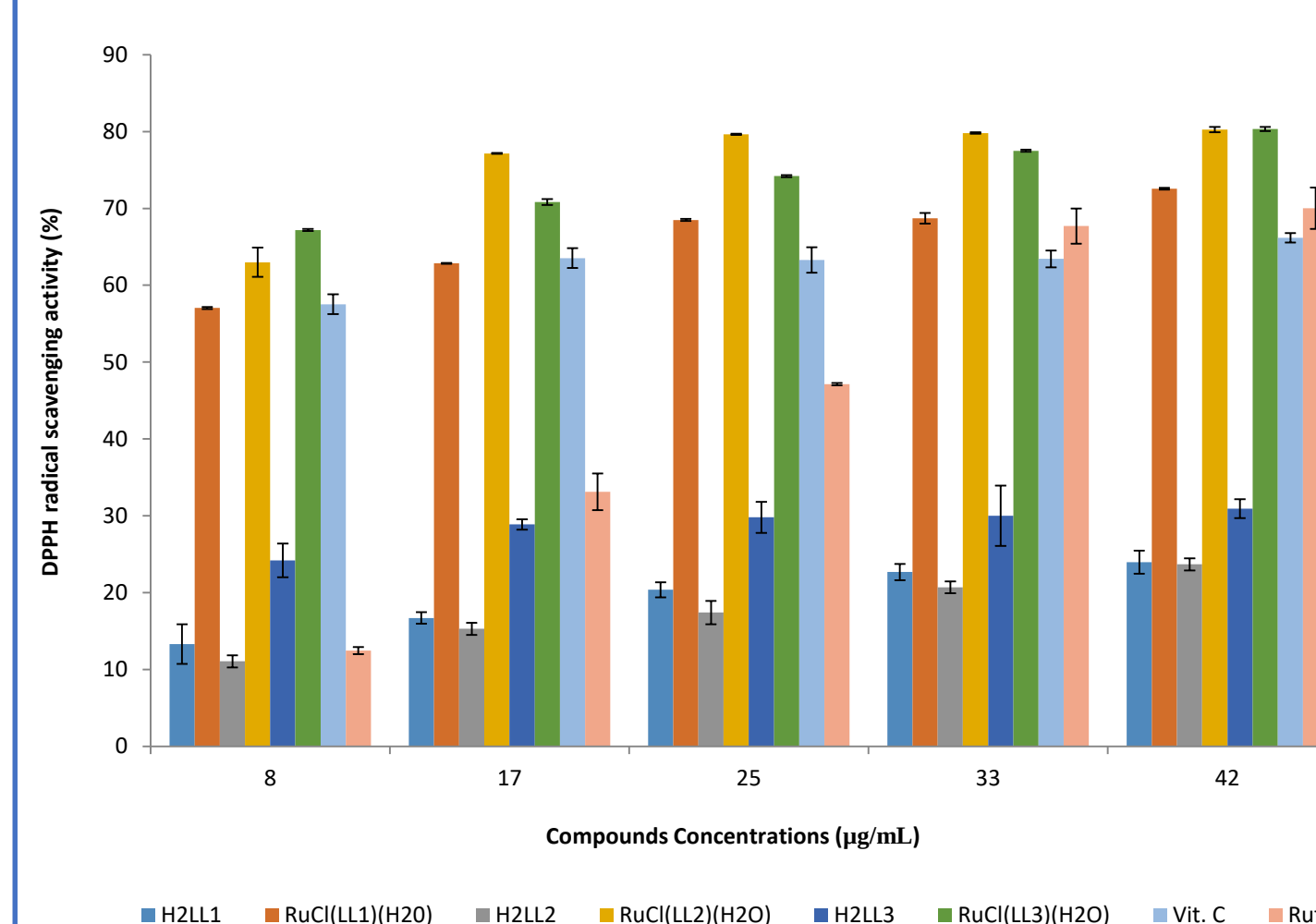


Electronic Spectra of [RuCl(LB)(H₂O)].2H₂O in DMF

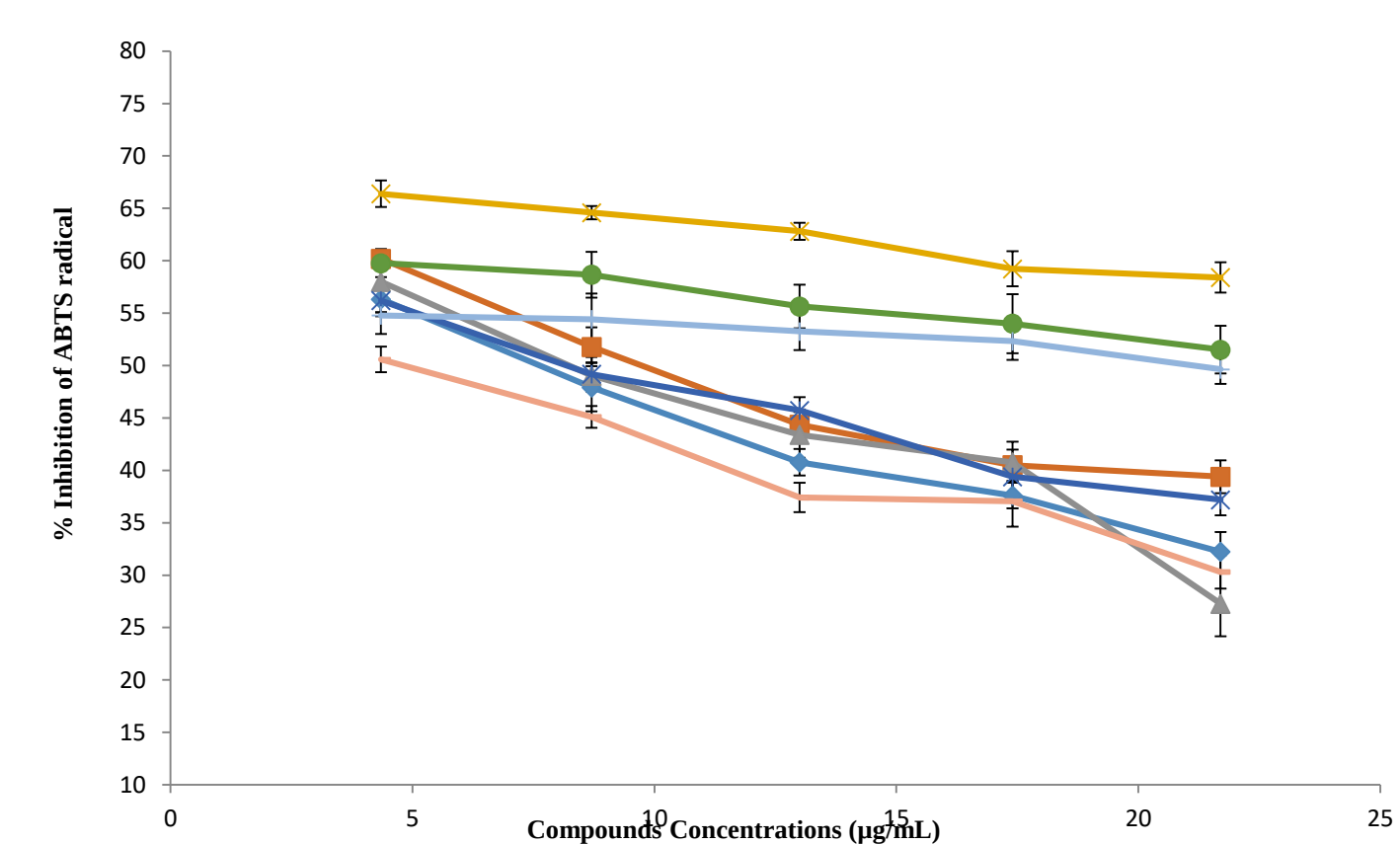
The antioxidant assay

Oxidative reactions of biological molecules has been revealed to induce a variety of pathological events such as cellular injury and ageing process, these damaging events are caused by free radicals. Therefore to prevent the free radical damage in the body, it is important to administer drugs or herbals that may be rich in antioxidants. The antioxidant activity of organic ligand and their metal complexes have gained wide interests, they have been investigated using the *in vitro* method [2, 5].

The Ru(III) complexes showed comparable or higher scavenging activity to the standards (Ascorbic acid and Rutin), with RuCl(LB) (H₂O) showed significantly higher scavenging ability. The 2,2-Diphenyl-1-picrylhydrazyl (DPPH) radical scavenging ability of the Ru(III) complexes can be ranked in the order: RuCl(LB)(H₂O) > RuCl(LC)(H₂O) > RuCl(LA)(H₂O). The LA, LB, LC ligands and their Ru complexes exhibited low to moderate scavenging ability of the 2,2-azinobis-(3-ethylbenzothiazoline-6-sulfonic acid (ABTS) radical and showed comparable or slightly less activity to that of Rutin and BHT (standard drugs).



DPPH scavenging activity N₂O₂ Schiff Bases and their Ru complexes



ABTS scavenging activity N₂O₂ Schiff Bases and their Ru complexes

Antiproliferative activity evaluation

The *in vitro* anticancer activities of Ru(III) complexes (at various concentrations ranging from 0.01 to 100 µM) were evaluated using three cancer cell lines: human renal cancer cell (TK10), human melanoma cancer cell (UACC62), and human breast cancer cell (MCF7) using the SRB assay and parthenolide was used as standard. [RuCl(LA)(H₂O)].2H₂O displayed non-selective antiproliferative activity against all tumor cells tested, while [RuCl(LB)(H₂O)].2H₂O and [RuCl(LC)(H₂O)].2H₂O had a low antiproliferative effect with IC₅₀ at 90 µM against MCF-7 (Z' factor > 0.5). The inhibition effects were enhanced by increasing the concentration of the Ru(III) complexes. The results showed that [RuCl(LB)(H₂O)].2H₂O was more active against all the selected tumor cells than [RuCl(LA)(H₂O)].2H₂O and [RuCl(LC) (H₂O)].2H₂O (Z' factor > 0.5).

IC₅₀ values (µM) of Ru(III) complexes and parthenolide against human cell lines*.

Compounds	Antiproliferative activity IC ₅₀ (µM) 48 h		
	TK-10	UACC-62	MCF-7
[RuCl(LA)(H ₂ O)].2H ₂ O	>100	>100	>100
[RuCl(LB)(H ₂ O)].2H ₂ O	>100	>100	90 ± 8
[RuCl(LC)(H ₂ O)].2H ₂ O	>100	>100	90 ± 5
Parthenolide	4.64 ± 1.43	11.37 ± 2.18	3.52 ± 2.02

*Cell described in Is were treated with various concentrations of tested compounds for 48 h. Each value represents the mean ± SD of three independent experiments (Z' factor > 0.5).

CONCLUSION

Ru(III) complexes of symmetric and asymmetric Schiff base ligands derived from ethane-1,2-diamine, 4-acetylresorcinol, acetylacetone, and 1-phenylbutane-1,3-dione were synthesized and characterized. Conductance measurements revealed non-electrolytes. Octahedral geometry around the Ru(III) ions is completed by H₂O and a Cl⁻. *In vitro* anticancer studies of the Ru complexes show that they are inactive against human cancer cells (TK10) and human melanoma cancer cell (UACC62) but show mild activity against human breast cancer cell line (MCF7). The synthesized complexes exhibited low biological activities as potential anticancer agents. Derivatization of the Schiff base by substituting CH₃ on the C2 and C4 position of acetylacetone could increase the activity of the complexes. Nevertheless, antioxidant activities of the complexes exhibited moderate to strong free radical inhibitors or scavenger for treating pathological damage associated with radical generation.

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