We are IntechOpen, the world's leading publisher of Open Access books Built by scientists, for scientists

6,900
Open access books available

185,000
International authors and editors

200M
Downloads

Our authors are among the

154
Countries delivered to

TOP 1%
most cited scientists

12.2%
Contributors from top 500 universities



WEB OF SCIENCE™

Selection of our books indexed in the Book Citation Index in Web of Science™ Core Collection (BKCI)

Interested in publishing with us?
Contact book.department@intechopen.com

Numbers displayed above are based on latest data collected.
For more information visit www.intechopen.com



15

From Synthesis to Antibacterial Activity of Some New Palladium(II) and Platinum(IV) Complexes

Ivana D. Radojević[1], Verica V. Glođović[2],
Gordana P. Radić[2], Jelena M. Vujić[3],
Olgica D. Stefanović[1], Ljiljana R. Čomić[1] and Srećko R. Trifunović[2]
[1]*Department of Biology and Ecology,*
Faculty of Science, University of Kragujevac, Kragujevac,
[2]*Department of Chemistry, Faculty of Science, University of Kragujevac, Kragujevac,*
[3]*Faculty of Agronomy, University of Kragujevac, Čačak,*
Republic of Serbia

1. Introduction

Simultaneously with the rapid development of a wide range of antibacterial agents since the 1940s, bacteria have proved extremely adept at developing resistance to each new employed agent. The rapidly increasing incidence of bacterial resistance to antimicrobial agents has become a serious problem worldwide. Resistance mechanisms have been identified and described for all known antibiotics currently available for clinical use (Fluit et al., 2000).

The synthesis and evaluation of the biological activity of the new metal-based compounds is the field of growing interest. Numerous complexes based on palladium(II) and platina(IV)-ion have been synthesized and their different biological activities have been documented (Agarwal, 2007; Mishra et al., 2007a; Mishra & Kaushik, 2007). The impact of different palladium and platinum complexes on the growth and metabolism of various groups of microorganisms has been studied. Garoufis et al. (2009) reviewed numerous scientific papers on anti-viral, antibacterial and antifungal activity of palladium(II) complexes with different types of ligands (sulfur and nitrogen donor ligands, Schiff base ligands and drugs as ligands). There are other papers in the literature showing different intensity of palladium(II) and platina(IV) complexes activity on various species of bacteria and fungi (Kovala-Demertzi et al., 2001; Brudzinska et al., 2004; Coombs et al., 2005; Guerra et al., 2005; Ali et al., 2006; Manav et al., 2006; Aghatabay et al., 2007; Kizilcikli et al., 2007; Mishra et al., 2007b; Biyala et al., 2008; Al-Hazmi et al., 2008; Vieira et al., 2009).

The aim of this paper is to describe synthesis of some new palladium(II) and platinum(IV) complexes and in vitro research of their antibacterial activities. The second objective is to evaluate the impact these compounds have on probiotic bacteria. Probiotics are used as supplements and they play significant role in protecting and maintaining the balance of intestinal microflora in antibiotic therapy.

2. Experimental

2.1 Chemistry

The palladium(II) and platinum(IV) complexes were obtained by direct reaction of the corresponding starting compounds (K_2PdCl_4 and K_2PtCl_6) and newly synthesized tetradentate or bidentate ligands. The next compounds were synthesized:

- *O,O'*-dipropyl-(*S,S*)-ethylenediamine-*N,N'*-di-2-propanoate (**L1**)
- dichlorido-(*O,O'*-dipropyl-(*S,S*)-ethylenediamine-*N,N'*-di-2-propanoate)-palladium(II) (**C1**)
- *O,O'*-dibutyl-(*S,S*)-ethylenediamine-*N,N'*-di-2-propanoate (**L2**)
- dichlorido-(*O,O'*-dibutyl-(*S,S*)-ethylenediamine-*N,N'*-di-2-propanoate)-palladium(II) (**C2**)
- *O,O'*-dipentyl-(*S,S*)-ethylenediamine-*N,N'*-di-2-propanoate (**L3**)
- dichlorido-(*O,O'*-dipentyl-(*S,S*)-ethylenediamine-*N,N'*-di-2-propanoate)-palladium(II) (**C3**)
- *O,O'*-ethyl-(*S,S*)-ethylenediamine-*N,N'*-di-2-(3-methyl)-butanoate (**L4**)
- chorido((*S,S*)-ethylenediamine-*N*-(*O*-ethyl-2-(3-methyl)-butanoate)-*N'*-2-(3-methyl)-butanoato)-palladium(II) (**C4**)
- tetrachlorido(*O,O'*-diethyl-(*S,S*)-ethylenediamine-*N,N'*-di-2-(3-methyl)butanoate)-platinum(IV) (**C4a**)
- *O,O'*-dipropyl-(*S,S*)-ethylenediamine-*N,N'*-di-2-(3-methyl)-butanoate (**L5**)
- chorido((*S,S*)-ethylenediamine-*N*-(*O*-propyl-2-(3-methyl)-butanoate)-*N'*-2-(3-methyl)-butanoato)-palladium(II) (**C5**)
- *O,O'*-dibutyl-(*S,S*)-ethylenediamine-*N,N'*-di-2-(3-methyl)-butanoate (**L6**)
- chorido((*S,S*)-ethylenediamine-*N*-(*O*-butyl-2-(3-methyl)-butanoate)-*N'*-2-(3-methyl)-butanoato)-palladium(II) (**C6**)
- *O,O'*-dipentyl-(*S,S*)-ethylenediamine-*N,N'*-di-2-(3-methyl)-butanoate(**L7**)
- chorido((*S,S*)-ethylenediamine-*N*-(*O*-pentyl-2-(3-methyl)-butanoate)-*N'*-2-(3-methyl)-butanoato)-palladium(II) (**C7**)
- *O,O'*-diethyl-(*S,S*)-ethylenediamine-*N,N'*-di-2-(4-methyl)-pentanoate (**L8**)
- dichlorido(*O,O'*-diethyl-(*S,S*)-ethylenediamine-*N,N'*-di-2-(4-methyl)-pentanoate)-palladium(II) (**C8**)
- *O,O'*-dipropyl-(*S,S*)-ethylenediamine-*N,N'*-di-2-(4-methyl)-pentanoate (**L9**)
- dichlorido(*O,O'*-dipropyl-(*S,S*)-ethylenediamine-*N,N'*-di-2-(4-methyl)-pentanoate)-palladium(II) (**C9**)
- *O,O'*-dibutyl-(*S,S*)-ethylenediamine-*N,N'*-di-2-(4-methyl)-pentanoate (**L10**)
- dichlorido(*O,O'*-dibutyl-(*S,S*)-ethylenediamine-*N,N'*-di-2-(4-methyl)-pentanoate)-palladium(II) (**C10**)
- *O,O'*-dipentyl-(*S,S*)-ethylenediamine-*N,N'*-di-2-(4-methyl)-pentanoate(**L11**) - dichlorido(*O,O'*-dipentyl-(*S,S*)-ethylenediamine-*N,N'*-di-2-(4-methyl)-pentanoate)-palladium(II) (**C11**)
- S-benzyl-thiosalicylic acid (**L12**)
- *bis*-(S-benzyl-thiosalicylate)-palladium(II) (**C12**)
- S-methyl-thiosalicylic acid (**L13**)

- *bis*-(S-methyl-thiosalicylate)-palladium(II) (**C13**)
- S-ethyl-thiosalicylic acid (**L14**)
- *bis*-(S-ethyl-2-thiosalicylate)-palladium(II) complex (**C14**)
- S-propyl-thiosalicylic acid (**L15**)
- *bis*-(S-propyl-2-thiosalicylate)-palladium(II) (**C15**)
- S-buthyl-thiosalicylic acid (**L16**)
- *bis*-(S-butyl-2-thiosalicylate)-palladium(II) (**C16**)
- *meso*-1,2-diphenyl-ethylenediamine-*N,N*'-di-3-propanoic acid (**L17**)
- dichlorido-(*meso*-1,2-diphenyl-ethylenediamine-*N,N*'-di-3-propanoate)-palladium(II) (**L17a**)
- *s-cis*-dichlorido-(*meso*-1,2-diphenyl-ethylenediamine-*N,N*'-di-3-propanoate)-platinum(IV) (**L17b**)
- *O,O*'-diethyl-(*S,S*)-ethylenediamine-*N,N*'-di-2-propanoate (**L18**)
- tetrachlorido(*O,O*'-diethyl-(*S,S*)-ethylenediamine-*N,N*'-di-2-propanoate)-platinum(IV)(**C18**)
- *O,O*'-diethyl-ethylenediamine-*N,N*'-di-*S,S*-(2,2'-benzyl)acetate (**L19**)
- tetrachorido(*O,O*'-diethyl-ethylenediamine-*N,N*'-di-*S,S*-(2,2'-benzyl)acetate)-platinum(IV) (**C19**)
- *O,O*'-dipropyl-ethylenediamine-*N,N*'-di-*S,S*-(2,2'-benzyl)acetate (**L20**)
- tetrachorido(*O,O*'-dipropyl-ethylenediamine-*N,N*'-di-*S,S*-(2,2'-benzyl)acetate)-platinum(IV) (**C20**)
- *O,O*'-dibutyl-ethylenediamine-*N,N*'-di-*S,S*-(2,2'-benzyl)acetate (**L21**)
- tetrachorido(*O,O*'-dibutyl-ethylenediamine-*N,N*'-di-*S,S*-(2,2'-benzyl)acetate)-platinum(IV) (**C21**)

2.1.1 The synthesis of the ligands - L1, L2, L3 and corresponding palladium(II) complexes – C1, C2, C3

In 50 mL of dry alcohol (1-propanol, 1-butanol or 1-pentanol), saturated with gas HCl, 1.53 g (7.5 mmol) of H_2-*S,S*-eddp was added and the mixture was refluxed for 12 h. The mixture was filtered and left in the refrigerator over night. The obtained white powder was filtered and air-dried.

Complexes were obtained by mixing $K_2[PdCl_4]$ (0.200 g, 0.613 mmol) and equimolar amount of the dpr-*S,S*-eddp·2HCl·3H_2O (**L1**) (0.2546 g, 0.613 mmol), dbu-*S,S*-eddp·2HCl·3H_2O (**L2**) (0.2718 g, 0.613 mmol) or dpe-*S,S*-eddp·2HCl·2H_2O (**L3**) (0.2780 g, 0.613 mmol) esters. During 2 h of stirring 10 cm^3 of water solution of LiOH (0.0294 g, 1.226 mmol) was added in small portions to the reaction mixture. Within this period, pale yellow precipitates of the complexes **C1-C3** were obtained, filtered off, washed with cold water, ethanol and ether and air dried (Vasić et al., 2010) (Fig. 1.).

2.1.2 The synthesis of the ligands - L4, L5, L6, L7 and corresponding palladium(II) complexes – C4, C5, C6, C7

In 50 mL of dry alcohol (ethanol, 1-propanol, 1-butanol or 1-pentanol), saturated with gas HCl, 2.50 g (7.5 mmol) of (H_2-(*S,S*)-eddv) was added and the mixture was refluxed for 12 h. The mixture was filtered off and the filtrate was left for a few days in a refrigerator at 4°C. The esters were recrystallized from hot alcohol used for each reaction.

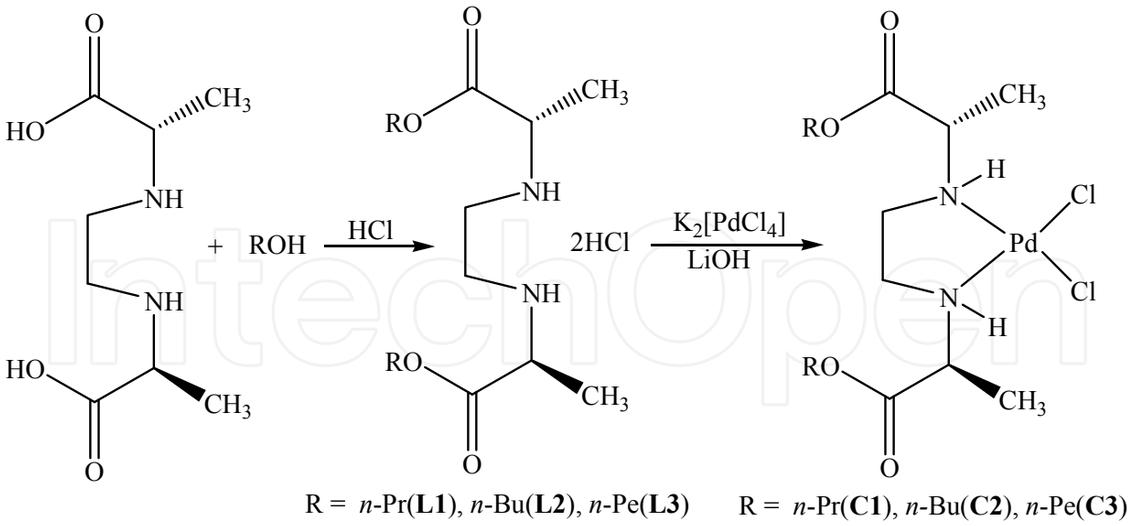


Fig. 1. The preparation of some alkyl esters of H_2-*S,S*-eddp and corresponding palladium(II) complexes

Complexes were obtained by mixing $K_2[PdCl_4]$ (0.200 g, 0.613 mmol) and equimolar amount of the **L4** (0.241 g, 0.613 mmol), **L5** (0.256 g, 0.613 mmol), **L6** (0.273 g, 0.613 mmol) or **L7** (0.290 g, 0.613 mmol) esters. During 2 h of stirring 10 cm^3 of water solution of LiOH (0.0294 g, 1.226 mmol) was added in small portions to the reaction mixture. Within this period, pale yellow precipitates of the complexes **C4-C7** were obtained, filtered off, washed with cold water, ethanol and ether and air dried (Fig.2.). The crystal structure of C4 was confirmed by X-ray analysis (Radić et al., 2010b; 2011a).

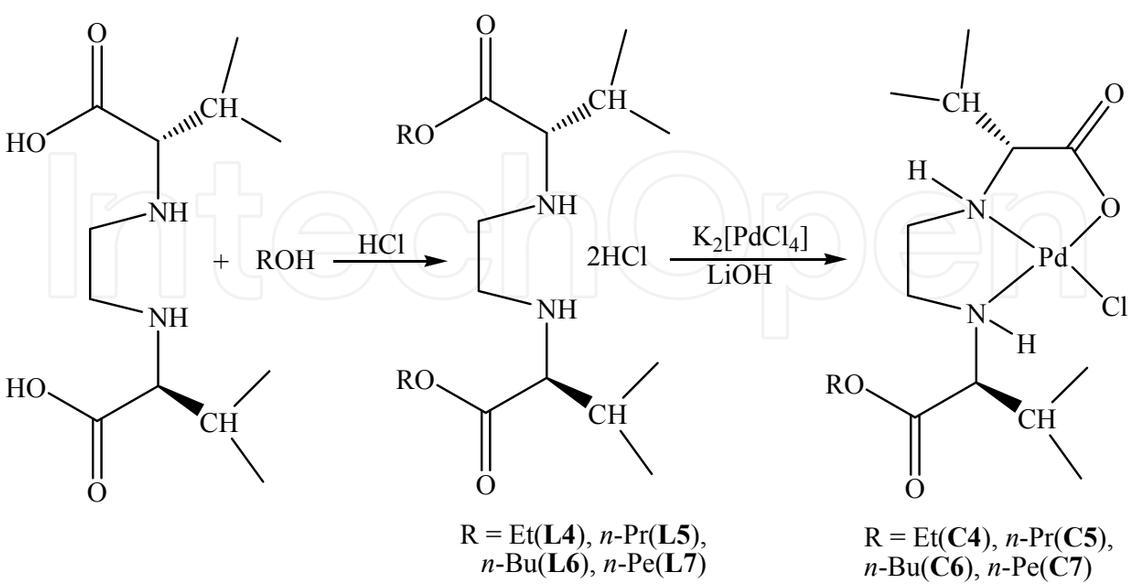


Fig. 2. The preparation of some alkyl esters of H_2-*S,S*-eddv and corresponding palladium(II) complexes

2.1.3 The synthesis of the ligands - L8, L9, L10, L11 and corresponding palladium(II) complexes – C8, C9, C10 and C11

Thionyl choride (4 cm^3, 55 mmol) was introduced into a flask containing 50 cm^3 of corresponding ice cooled alcohol (ethyl, *n*-propyl, n-butyl or *n*-pentyl; anhydrous conditions) for 1 h. After addition of 2 g (5.54 mmol) [(*S,S*)-H_4eddl]Cl_2 the reaction mixture was refluxed for 16 h, filtered off and the filtrate was left for a few days in a refrigerator at 4°C. The esters were recrystallized from the hot alcohol used for each reaction.

Complexes were obtained by mixing $K_2[PdCl_4]$ (0.2 g, 0.61 mmol) and equimolar amount of the **L8**·H_2O (0.267 g, 0.61 mmol), **L9**·H_2O (0.277 g, 0.61 mmol), **L10**·H_2O (0.301 g, 0.61 mmol) or **L11**·H_2O (0.318 g, 0.61 mmol) esters. During 2 h of stirring 10 cm^3 of water solution of LiOH (0.0293 g, 1.22 mmol) was added in small portions to the reaction mixture. Within this period, pale yellow precipitates of the complexes **C8-C11** were obtained, filtered off, washed with cold water, ethanol and ether and air dried (Vujić et al., 2010) (Fig.3.). The crystal structure of **C11** was confirmed by X-ray analysis (Vujić, et al., 2011).

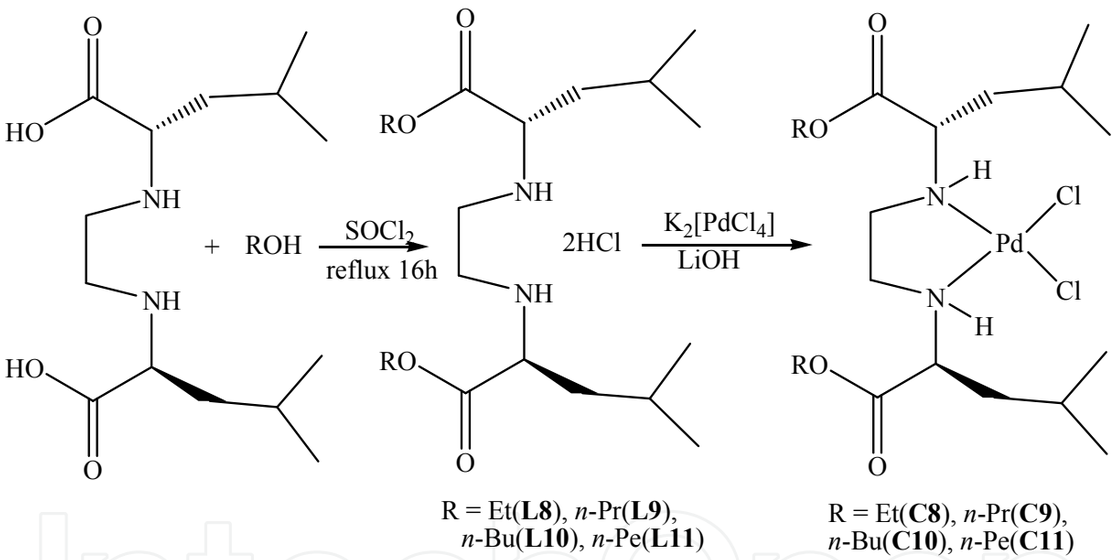


Fig. 3. The preparation of some alkyl esters of H_2-*S,S*-eddl and corresponding palladium(II) complexes

2.1.4 The synthesis of the ligands - L12, L13, L14, L15, L16 and corresponding palladium(II) complexes – C12, C13, C14, C15, C16

The thioacid ligands (**L12**)-(**L16**) were prepared by alkylation of thiosalicylic acid by means of corresponding alkyl halogenides in alkaline water-ethanol solution.

Thiosalicylic acid (1 mmol) was added to a 100 cm^3 round bottom flask containing 50 cm^3 of 30% solution of ethanol in water and stirred. A solution of NaOH (2 mmol in 5 cm^3 of water) was added to acid suspension. The solution became clear. The corresponding alkyl halogenide (2 mmol) was dissolved in 5 cm^3 of ethanol and transferred to the stirred solution. The resulting mixture was kept overnight at 60°C. The reaction mixture was

transferred into a beaker and ethanol was evaporated off on a water bath. Diluted hydrochloric acid (2 mol/dm^3) was added to the resulting water solution and S-alkyl thiosalicylic acid was precipitated as a white powder. The liberated acid was filtered off and washed with plenty of distilled water. The product was dried under vacuum overnight.

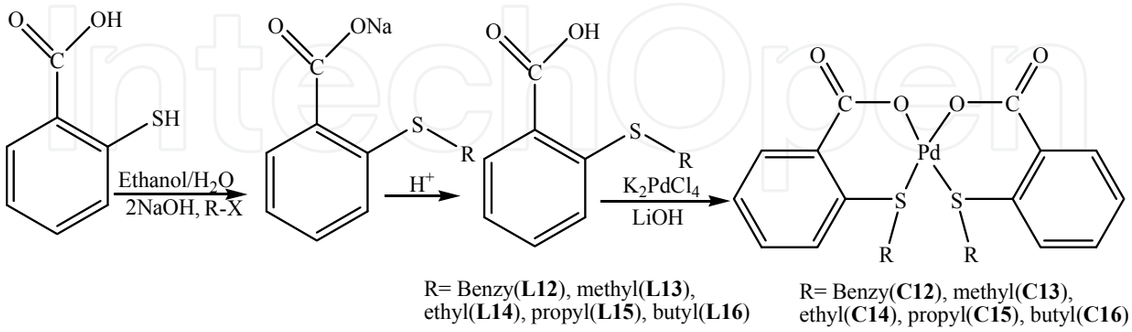


Fig. 4. The preparation of alkyl eters of 2-thiosalicylic acid and corresponding palladium(II) complexes

$K_2[PdCl_4]$ (0.100 g, 0.3065 mmol) was dissolved in 10 cm^3 of water on a steam bath and (S-benzyl)-2-thiosalicylic acid (0.1497 g, 0.613 mmol), (S-methyl)-2-thiosalicylic acid (0.103 g, 0.613 mmol), (S-ethyl)-2-thiosalicylic acid (0.1117 g, 0.613 mmol), (S-propyl)-2-thiosalicylic acid (0.1203 g, 0.613 mmol) or (S-butyl)-2-thiosalicylic acid, (0.1289 g, 0.613 mmol) was added into the solution. The resulting mixture was stirred for 2h and during this time an aqueous solution of LiOH (0.0256 g, 0.613 mmol in 10 cm^3 of water) was introduced. The complexes (**C12- C16**) as a yellow precipitate were filtered, washed with water and air-dried (Radić et al., 2011) (Fig.4.). The crystal structure of **C12** was confirmed by X-ray analysis (Dimitrijević et al., 2011).

2.1.5 The synthesis of the ligand L17 and corresponding palladium(II) complex C17 and corresponding platinum(IV) complex C17a

Benzaldehyde (30 g) was refluxed with ammonium acetate (60 g) for 3 hours. The reaction mixture was cooled and the product was filtered and washed with ethanol. Recrystallization from 1-butanol gave *N*-benzoyl-*N*'-benzylidene-*meso*-1,2-diphenyl-ethylendiamine. Hydrolysis of that compound with 70% sulphuric acid under reflux for 1h gave *meso*-1,2--diphenyl-ethylenediamine as the basic product of hydrolysis.

3-Chloro-propanoic acid (4.34 g, 0.04 mol) was dissolved in 5 cm^3 of water on ice bath and carefully neutralized with cold water solution of 5 cm^3 NaOH (1.6 g, 0.04 mol). 1,2-Diphenyl--ethylenediamine (4.24 g, 0.02 mol) was added to this solution. The mixture was being stirred for 4 hours at 90°C, and during this period 5 cm^3 NaOH water solution (1.6 g, 0.04 mol) was introduced. After that, 5.6 cm^3 6 mol/dm^3 HCl was added and resulting solution was evaporated to the volume of 7 cm^3; 6 cm^3 *conc.* HCl, 6 cm^3 of ethanol and 6 cm^3 of ether were added to the mixture. The white precipitate of H_2 -1,2-dpheddp·2HCl·1.5H_2O (**L17**) was separated by filtration and refined with solution water : ethanol = 1 : 2. The crystal structure of **L17** was confirmed by X-ray analysis (Radić et al., 2010a).

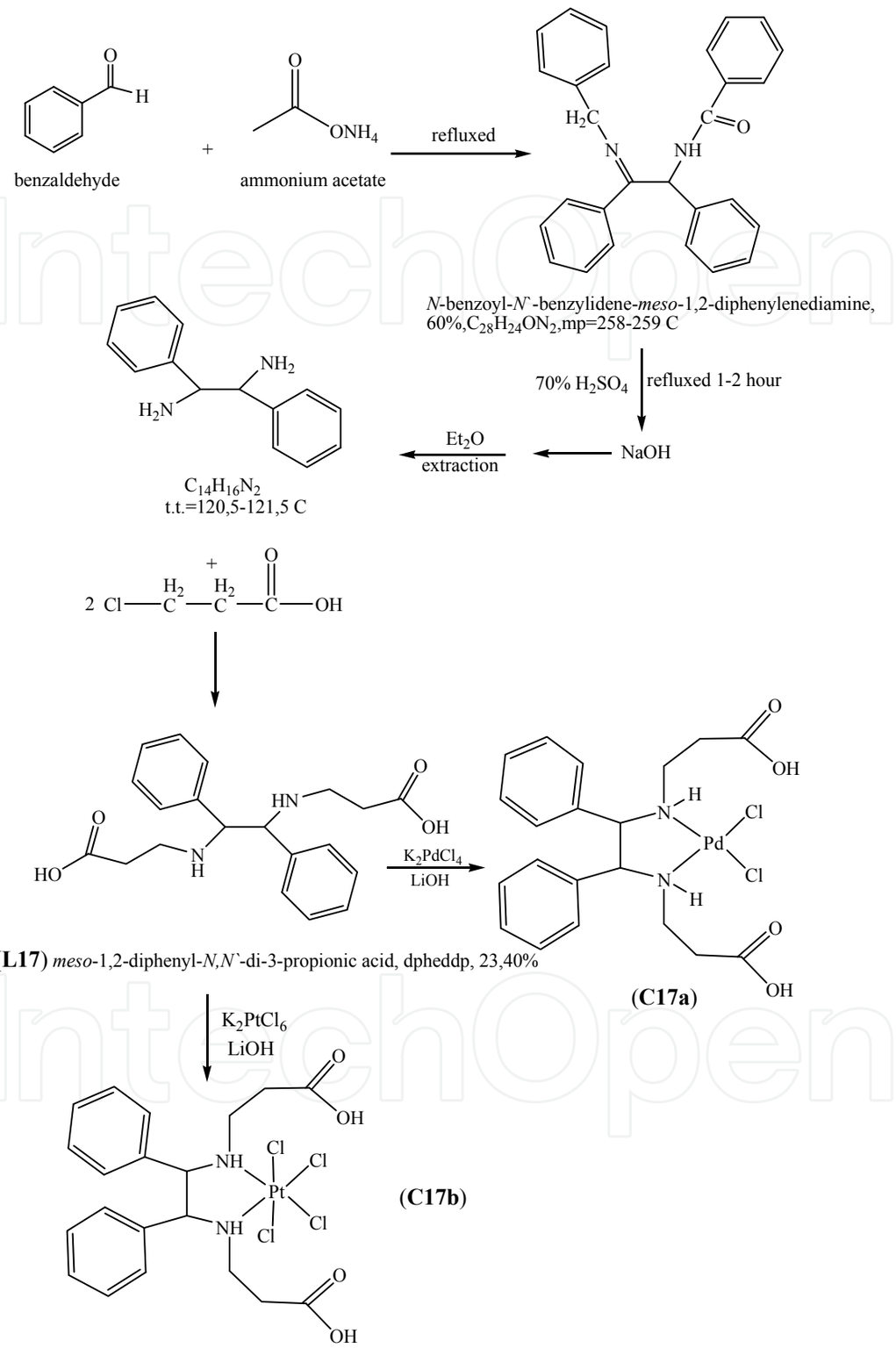


Fig. 5. Reaction pathways in synthesis of *meso*-1,2-diphenyl-ethylenediamine-*N,N*'-di-3--propionic acid and corresponding palladium(II) and platinum(IV) complexes.

Potassium-hexachloridoplatinate(IV) (0.2 g, 0.411 mmol) was dissolved in 10 cm^3 of water on a steam bath and 1,2-diphenyl-ethylenediamine-*N,N'*-di-3-propanoic acid (0.1876 g, 0.411 mmol) was added. The reaction mixture was heated for 12 hours and during this period 10 cm^3 of LiOH water solution (0.0394 g, 1.65 mmol) was added in small portions and the solution was filtered and evaporated to small volume. The orange precipitate of *s-cis*-[$PtCl_2$(1,2-dpheddp)] **C17b**) was separated by filtration, washed with cold water and air-dried (Fig. 5).

2.1.6 The synthesis of the ligands L4, L18 and corresponding platinum(IV) complexes C4a, C18

$K_2[PtCl_6]$ (0.100 g, 0.205 mmol) and det-(*S,S*)-eddv (0.080 g, 0.205 mmol) were dissolved in 25 cm^3 of water. The reaction mixture was heated on a steam bath for 3 h during which water solution of LiOH·H_2O (0.017 g, 0.41 mmol in 10 cm^3 of water) was introduced. The complex, [$PtCl_4$(det-(*S,S*)-eddv)] (**C4a**), as a yellow precipitate was separated by filtration, washed with water and air-dried (Fig. 6.).

In 50 cm^3 of dry ethanol, saturated with gas HCl, 1.53 g (7.5 mmol) of H_2-*S,S*-eddp was added and the mixture was refluxed for 12 h. The mixture was filtered and left in the refrigerator over night. The obtained white powder of *O,O'*-diethyl-(*S,S*)--ethylenediamine-*N,N'*-di-2-propanoate dihydrochloride, det-*S,S*-eddp·2HCl (**L18**) was filtered and air dried.

$K_2[PtCl_6]$ (0.100 g, 0.205 mmol) and det-(*S,S*)-eddp (0.068 g, 0.205 mmol) were dissolved in 25 cm^3 of water. The reaction mixture was heated on a steam bath for 3 h during which water solution of LiOH·H_2O (0.017 g, 0.41 mmol in 10 cm^3 of water) was introduced. The complex, [$PtCl_4$(det-(*S,S*)-eddp)] (**C18**), as a yellow precipitate was separated by filtration, washed with water and air-dried (Stanković et al., 2011b) (Fig. 7.). The crystal structure of **C18** was confirmed by X-ray analysis (Stanković et al., 2011b).

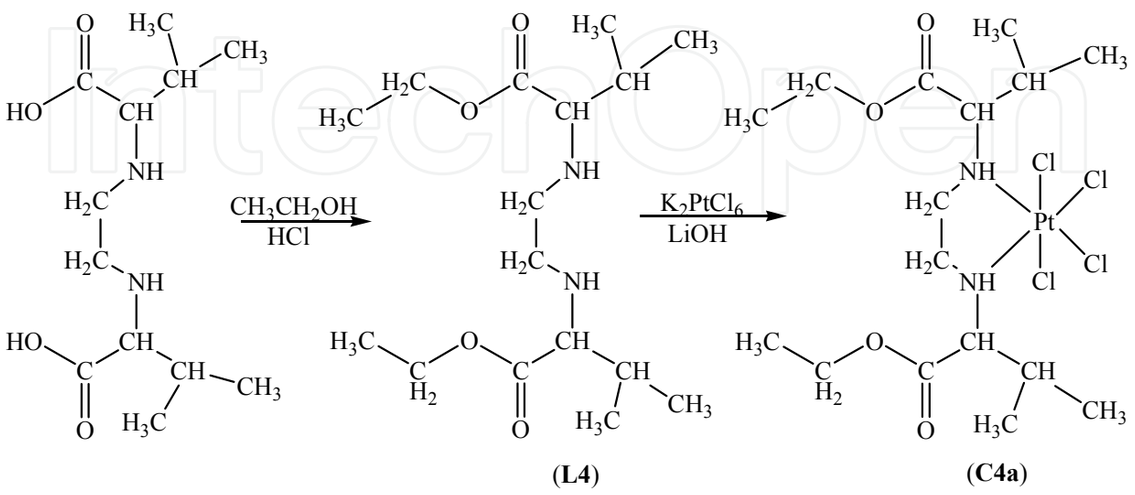


Fig. 6. Synthesis of the ester det-(*S,S*)-eddv·2HCl and platinum(IV) complex

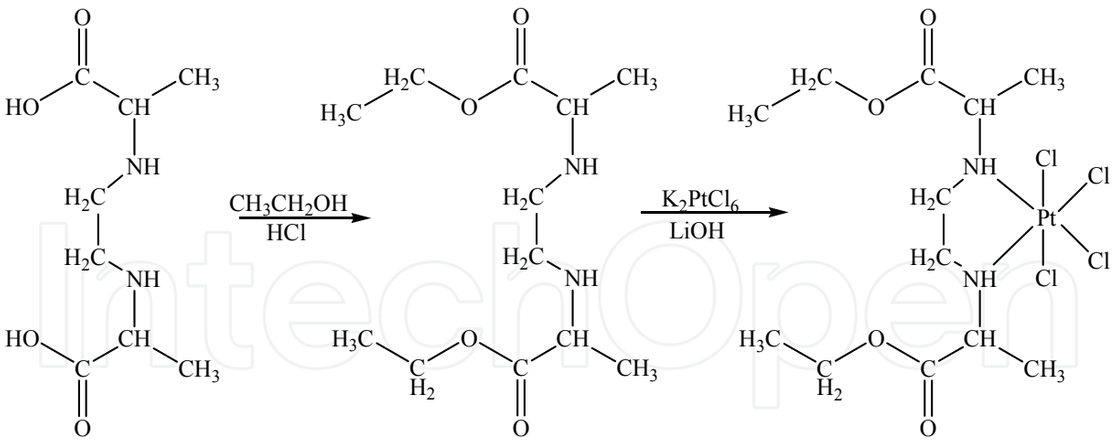
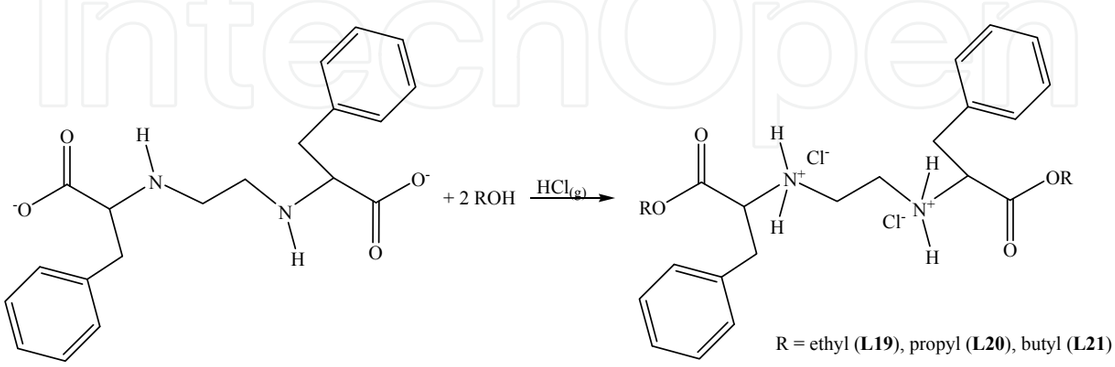


Fig. 7. Synthesis of the ester det-(*S,S*)-eddp ·2HCl and platinum(IV) complex

2.1.7 The synthesis of the ligands L19, L20, L21 and corresponding platinum(IV) complexes C19, C20, C21

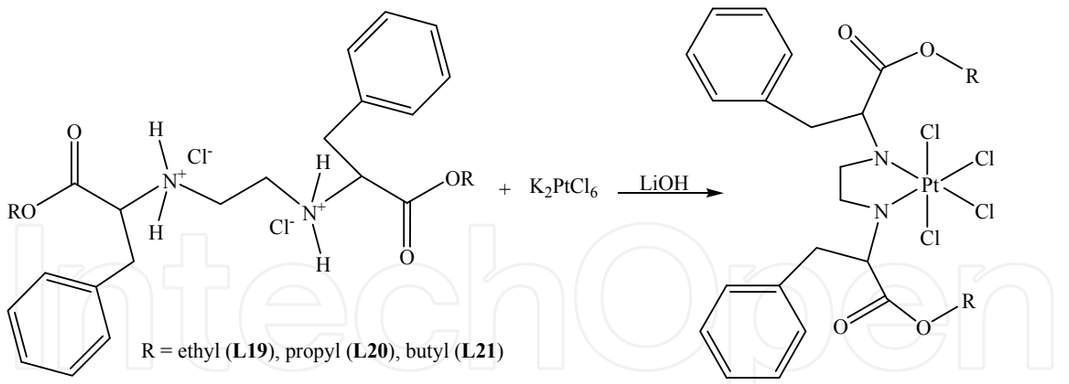
In 50 cm^3 of dry alcohol (ethanol, 1-propanol, 1-butanol) saturated with gaseous HCl, 1.50 g (3.65 mmol) of ethylenediamine-*N,N'*-di-*S,S*-(2,2′-dibenzyl)acetate acid threehydrate (H_2-*S,S*-eddba ·3H_2O) was added and the mixture was refluxed for 12 h. The mixture was filtered and left in the refrigerator over night. The obtained white powder was filtered and air-dried.

$K_2[PtCl_6]$ (0.100 g, 0.206 mmol) and 0.206 mmol of R_2-*S,S*-eddba ·2HCl (0.100 g of de-*S,S*--eddba ·2HCl (**L19**), 0.106 g of dp-*S,S*-eddba ·2HCl (**L20**), 0.112 g of db-*S,S*-eddba ·2HCl (**L21**)) were dissolved in 15 cm^3 of water. The reaction mixture was heated at 40 °C for 12 h and during this period 3.92 cm^3 of aqueous 0.105 mol/dm^3 LiOH ·H_2O (0.412 mmol) were added in small portions The complexes (**C19-C21**) as a yellow-orange precipitates were collected by filtration, washed with water, corresponding alcohol and ether and air-dried (Fig. 8.). The crystal structure of **L20** was confirmed by X-ray analysis (Dimitrijević et al., 2010).



H_2-*S,S*-eddba

a)



b)

Fig. 8. The synthesis of: a) esters (R_2-*S,S*-eddba·2HCl); b) complexes [$PtCl_4$(R_2-*S,S*-eddba)]

2.2 In vitro antimicrobial assay

2.2.1 Test substances

The tested compounds were dissolved in DMSO and then diluted into nutrient liquid medium to achieve a concentration of 10%. Antibiotic, doxycycline (Galenika A.D., Belgrade), was dissolved in nutrient liquid medium, a Mueller–Hinton broth (Torlak, Beograd).

2.2.2 Test microorganisms

Antimicrobial activity of twenty-one palladium(II) and platinum(IV) complexes and their ligands was tested against 9 species of bacteria: 6 strains of pathogenic bacteria (including 4 standard strains: *Pseudomonas aeruginosa* ATCC 27853, *Enterococcus faecalis* ATCC 29212, *Staphylococcus aureus* ATCC 25923; *Sarcina lutea* ATCC 9341 and 2 clinical isolates: *Escherichia coli* and *Salmonella enterica*) and 3 species of probiotic bacteria (*Bacillus subtilis* IP 5832 PMFKG-P32, *Bifidobacterium animalis subsp. lactis* PMFKG-P33 and *Lactobacillus rhamnosus* PMFKG-P35). All clinical isolates were a generous gift from the Institute of Public Health, Kragujevac. The other microorganisms were provided from a collection held by the Microbiology Laboratory Faculty of Science, University of Kragujevac.

2.2.3 Suspension preparation

Bacterial suspensions were prepared by the direct colony method. The colonies were taken directly from the plate and were suspended in 5 mL of sterile 0.85% saline. The turbidity of initial suspension was adjusted by comparing with 0.5 McFarland's standard (0.5 ml 1.17% w/v $BaCl_2 \times 2H_2O$ + 99.5 ml 1% w/v H_2SO_4) (Andrews, 2005). When adjusted to the turbidity of the 0.5 McFarland's standard, bacteria suspension contains about 10^8 colony forming unites (CFU)/mL. Ten-hold dilutions of initial suspension were additionally prepared into sterile 0.85% saline.

2.2.4 Microdilution method

Antimicrobial activity was tested by determining the minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) by using microdilution plate method

with resazurin (Sarker et al., 2007). The 96-well plates were prepared by dispensing 100 μL of nutrient broth into each well. A 100 μL from the stock solution of tested compound (concentration 2000 μg/mL) was added into the first row of the plate. Then, twofold, serial dilutions were performed by using a multichannel pipette. The obtained concentration range was from 1000 μg/mL to 7.81 μg/mL. A 10 μL of diluted bacterial suspension was added to each well to give a final concentration of 5 x 10^5 CFU/mL. Finally, 10 μL resazurin solution was added to each well inoculated with bacteria. Resazurin is an oxidation–reduction indicator used for the evaluation of microbial growth. It is a blue non-fluorescent dye that becomes pink and fluorescent when reduced to resorufin by oxidoreductases within viable cells (Banfi et al., 2003). The inoculated plates were incubated at 37 °C for 24 h. MIC was defined as the lowest concentration of the tested substance that prevented resazurin color change from blue to pink. Doxycycline was used as a positive control. Solvent control test was performed to study an effect of 10% DMSO on the growth of microorganism. It was observed that 10% DMSO did not inhibit the growth of microorganism. Also, in the experiment, the concentration of DMSO was additionally decreased because of the twofold serial dilution assay (the working concentration was 5% and lower). Each test included growth control and sterility control. All tests were performed in duplicate and MICs were constant. Minimum bactericidal concentration was determined by plating 10 μL of samples from wells, where no indicator color change was recorded, on nutrient agar medium. At the end of the incubation period the lowest concentration with no growth (no colony) was defined as minimum bactericidal concentration.

3. Results and discussion

The results of *in vitro* testing of antibacterial activities of the ligands and corresponding palladium(II) and platinum(IV) complex are shown in Table 1-10. For comparison, MIC and MBC values of doxycycline are listed in Table 11. The solvent (10% DMSO) did not inhibit the growth of the tested microorganisms.

The intensity of antimicrobial action varied depending on the species of microorganism and on the type and concentration of tested compounds. The difference between antimicrobial activity of the ligands and corresponding palladium(II) and platinum(IV) complexes is noticed and, in general, the most active were palladium(II) complexes.

The results of antibacterial testing for the ligands (**L1, L2, L3**) and corresponding palladium(II) complexes (**C1, C2, C3**) are shown in Table 1. The results for 3 strains of pathogenic bacteria and 2 species of probiotic bacteria were reported in the paper Vasić et al., (2010). Results for *S. enterica*, *Staphyl. aureus* ATCC 25923, *S. lutea* ATCC 9341 and *L. rhamnosus* were first presented in this paper. These ligands and complexes, being compared to positive control, showed low to moderate antibacterial activity. MIC and MBC values were in range from <7.81 to >1000 μg/mL, depending on the species of bacteria. Gram-positive bacteria showed higher sensitivity. The most sensitive was *S. lutea* ATCC 9341, where MIC was for **C1** and **C2** <7.81 μg/mL. The best activity at Gram-negative bacteria was shown by **C2** to *P. aeruginosa* ATCC 27853 and *E. coli* (MIC was 31.25 μg/mL). The probiotics showed sensitivity similar to the sensitivity of the other bacteria to the tested compounds. Exception is *B. animalis subsp. lactis* where **L2**, **C2** and **L3** inhibited its growth at these concentrations: 7.81 μg/mL, 15,63 μg/mL and <7.81 μg/mL.

The results of testing the ligands (**L4, L5, L6, L7**) and their palladium(II) complexes (**C4, C5, C6, C7**) are shown in Table 2 and Table 3. The results of testing for **L4** were reported in the paper by Stanković et al., (2011a; 2011c). The tested ligands, with few exceptions, show very low antimicrobial activity, while palladium(II) complexes show selective and moderate activity. Interestingly, **L6**, **L7** and **C6**, **C7** exhibit strong antibacterial activity towards *E. coli*, *Staphyl. aureus* ATCC 25923 and *S. lutea* ATCC 9341, MIC ranged <7.81 μg/mL to 31.25μg/mL. Probiotic bacteria showed high resistance to the effects of tested substances. The most sensitive was *B. subtilis* IP 5832 to **C5** and **C4** (MIC was 7.81μg/mL and 15.63 μg/mL).

The results of testing the ligands (**L8, L9, L10, L11**) and palladium(II) complexes (**C8, C9, C10, C11**) are shown in Table 4 and Table 5. The ligands and complexes, being compared to positive control, with few exceptions, showed low antibacterial activity. MIC and MBC values were in range from <7.8 to >1000 μg/mL, depending on the species of bacteria. **L9**, **L10** and **L11** showed excellent results to *S. lutea* ATCC 9341 (MIC and MBC <7.81 μg/mL) and **L10** and **L11** to *S. lutea* ATCC 9341, *Staphyl. aureus* ATCC 25923 and *L. rhamnosus* (MIC <7.81 μg/mL). In this case the ligands acted better than corresponding complexes and it is an exception. The complexes have weak antimicrobial activity and some better influence was seen on *B. subtilis* IP 5832 were MIC was in range from 39.06 to 312.5 μg/mL.

The results of testing the ligands (**L12, L13, L14, L15, L16**) and corresponding palladium (II) complexes (**C12, C13, C14, C15, C16**) are shown in Table 6 and Table 7. The results for these testing were accepted for publication in the paper by Radić et al., (2011b). All tested compounds demonstrated selective and moderate antibacterial activity. Tested ligands, with a few exceptions, show very low antimicrobial activity. The activity of corresponding complexes was higher than with the ligands. MICs values for ligands were in range from 250 μg/mL to >1000 μg/mL, and for complexes from 62.5 μg/mL to 1000 μg/mL. The Gram-positive bacteria were more sensitive than the Gram-negative bacteria especially by the activity of the complexes. The best effect was observed in **C16** to *S. lutea* ATCC 9341 were MIC and MBC 62.5 μg/mL. MICs for Gram-negative bacteria were at 500 μg/mL and 1000 μg/mL. The tested complexes (**C13**) and (**C14**) exhibited somewhat stronger antibacterial activity towards *P. aeruginosa* ATCC 27853 (MIC = 250 μg/mL). The probiotics showed sensitivity similar to the sensitivity of the other bacteria (Radić et al., 2011b).

Species	L1		C1		L2		C2		L3		C3	
	MIC	MBC	MIC	MBC	MIC	MBC	MIC	MBC	MIC	MBC	MIC	MBC
Escherichia coli [1]	125	>500	62,5	125	31.3	>500	31,25	> 250	250	>500	125	> 500
Salmonella enterica	>1000	>1000	125	125	nt	nt	250	500	1000	>1000	250	500
Pseud. aeruginosa ATCC 27853 [1]	>500	>500	125	250	>500	>500	31,25	125	250	>500	125	125
Enter. faecalis ATCC 29212 [1]	>500	>500	125	250	125	>500	62,5	250	>500	>500	62,5	250
Staphyl. aureus ATCC 25923	>1000	>1000	62.5	125	nt	nt	62.5	125	250	1000	62.5	125
Sarcina lutea ATCC 9341	1000	1000	<7.8	<7.8	nt	nt	<7.8	15,6	31,25	125	31,25	31,25
Lactobacillus rhamnosus	nt	nt	62.5	500	nt	nt	62.5	250	nt	nt	62.5	125
Bifidobact. animalis subsp. lactis [1]	125	>500	62,5	125	7.81	>500	15,6	125	<7.81	< 31.25	125	> 500
Bacillus subtilis IP 5832 [1]	125	>500	62,5	125	62.5	>500	15,6	125	62.5	>500	62,5	> 500

MIC, minimum inhibitory concentration (μg/mL),
MBC, minimum bactericidal concentration (μg/mL), nt, not tested

Table 1. Antibacterial activity of the ligands (**L1,L2,L3**) and corresponding complexes (**C1, C2, C3**).

[1] Vasić et al., (2010)

Species	L4 [2]		C4		L5		C5	
	MIC	MBC	MIC	MBC	MIC	MBC	MIC	MBC
Escherichia coli	500	1000	125	500	125	1000	125	500
Salmonella enterica	1000	>1000	1000	1000	>1000	>1000	1000	1000
Pseud. aeruginosa ATCC 27853	1000	1000	500	1000	>1000	>1000	500	1000
Enter. faecalis ATCC 29212	500	500	500	1000	>1000	>1000	500	>1000
Staphyl. aureus ATCC 25923	500	500	250	500	250	500	125	500
Sarcina lutea ATCC 9341	31.25	125	250	250	1000	1000	250	250
Lactobacillus rhamnosus	1000	1000	500	1000	nt	nt	500	1000
Bifidobact. animalis subsp. lactis	250	500	125	1000	500	>1000	250	>1000
Bacillus subtilis IP 5832	125	500	15.63	>1000	62.5	>1000	7.81	1000

MIC, minimum inhibitory concentration (μg/mL),
MBC, minimum bactericidal concentration (μg/mL), nt, not tested

Table 2. Antibacterial activity of the ligands (**L4, L5**) and corresponding complexes (**C4, C5**).

Species	L6		C6		L7		C7	
	MIC	MBC	MIC	MBC	MIC	MBC	MIC	MBC
Escherichia coli	15.63	500	31.25	500	15.63	125	<7.81	125
Salmonella enterica	1000	1000	250	500	1000	1000	1000	1000
Pseud. aeruginosa ATCC 27853	>1000	>1000	500	1000	500	>1000	500	1000
Enter. faecalis ATCC 29212	1000	>1000	500	1000	1000	>1000	500	1000
Staphyl. aureus ATCC 25923	31.25	125	125	125	31.25	125	500	500
Sarcina lutea ATCC 9341	31.25	31.25	31.25	31.25	<7.81	<7.81	250	250
Lactobacillus rhamnosus	31.25	250	62.50	125	62.50	250	500	1000
Bifidobact. animalis subsp. lactis	62.50	1000	62.50	1000	62.50	500	125	>1000
Bacillus subtilis IP 5832	250	>1000	500	1000	1000	>1000	500	>1000

MIC, minimum inhibitory concentration (μg/mL),
MBC, minimum bactericidal concentration (μg/mL)

Table 3. Antibacterial activity of the ligands (**L6, L7**) and corresponding complexes (**C6, C7**).

Species	L8		C8		L9		C9	
	MIC	MBC	MIC	MBC	MIC	MBC	MIC	MBC
Escherichia coli	625	>1000	625	>1000	312.5	>1000	>1000	>1000
Salmonella enterica	>1000	>1000	>1000	>1000	>1000	>1000	>1000	>1000
Pseud. aeruginosa ATCC 27853	>1000	>1000	>1000	>1000	>1000	>1000	>1000	>1000
Enter. faecalis ATCC 29212	>1000	>1000	>1000	>1000	>1000	>1000	625	>1000
Staphyl. aureus ATCC 25923	250	500	500	1000	31.25	125	250	500
Sarcina lutea ATCC 9341	250	250	500	500	<7.8	<7.8	250	250
Lactobacillus rhamnosus	1000	1000	500	1000	15.63	125	500	1000
Bifidobact. animalis subsp. lactis	78	>1000	78	>1000	>1000	>1000	>1000	>1000
Bacillus subtilis IP 5832	78.13	>1000	39.06	625	625	>1000	78	>1000

MIC, minimum inhibitory concentration (μg/mL),
MBC, minimum bactericidal concentration (μg/mL)

Table 4. Antibacterial activity of the ligands (**L8, L9**) and corresponding complexes (**C8, C9**).

[2] Stanković et al., (2011a, 2011c)

Species	L10		C10		L11		C11	
	MIC	MBC	MIC	MBC	MIC	MBC	MIC	MBC
Escherichia coli	>1000	>1000	>1000	>1000	625	>1000	312.5	>1000
Salmonella enterica	>1000	>1000	>1000	>1000	>1000	>1000	>1000	>1000
Pseud. aeruginosa ATCC 27853	>1000	>1000	>1000	>1000	>1000	>1000	312.5	>1000
Enter. faecalis ATCC 29212	156.3	>1000	625	>1000	>1000	>1000	156.3	>1000
Staphyl. aureus ATCC 25923	<7.8	125	31.25	125	<7.8	125	500	500
Sarcina lutea ATCC 9341	<7.8	<7.8	31.25	31.25	<7.8	<7.8	250	250
Lactobacillus rhamnosus	<7.8	<7.8	31.25	62.5	<7.8	<7.8	500	1000
Bifidobact. animalis subsp. lactis	>1000	>1000	>1000	>1000	>1000	>1000	625	>1000
Bacillus subtilis IP 5832	>1000	>1000	78	>1000	>1000	>1000	312.5	>1000

MIC, minimum inhibitory concentration (μg/mL),
MBC, minimum bactericidal concentration (μg/mL)

Table 5. Antibacterial activity of the ligands (**L10, L11**) and corresponding complexes (**C10,C11**).

Species	L12		C12		L13		C13		L14		C14	
	MIC	MBC	MIC	MBC	MIC	MBC	MIC	MBC	MIC	MBC	MIC	MBC
Escherichia coli	>1000	>1000	1000	1000	1000	>1000	500	500	1000	>1000	500	500
Salmonella enterica	1000	>1000	1000	1000	1000	>1000	500	500	1000	>1000	500	500
Pseud. aeruginosa ATCC 27853	500	>1000	500	1000	500	>1000	250	500	500	>1000	250	500
Enter. faecalis ATCC 29212	1000	1000	500	500	1000	1000	500	1000	500	1000	250	500
Staphyl. aureus ATCC 25923	500	1000	500	1000	1000	1000	500	1000	1000	1000	500	500
Sarcina lutea ATCC 9341	250	500	250	250	1000	1000	250	250	500	500	250	500
Lactobacillus rhamnosus	>1000	>1000	1000	1000	1000	>1000	500	1000	1000	1000	500	500
Bifidobact. animalis subsp. lactis	500	500	500	1000	500	500	1000	1000	1000	1000	500	500
Bacillus subtilis IP 5832	500	500	500	500	500	500	500	500	1000	>1000	250	500

MIC, minimum inhibitory concentration (μg/mL),
MBC, minimum bactericidal concentration (μg/mL)

Table 6. [3] Antibacterial activity of the ligands (**L12, L13, L14**) and corresponding complexes (**C12, C13, C14**).

Species	L15		C15		L16		C16	
	MIC	MBC	MIC	MBC	MIC	MBC	MIC	MBC
Escherichia coli	1000	>1000	500	500	>1000	>1000	1000	1000
Salmonella enterica	1000	>1000	500	1000	>1000	>1000	1000	1000
Pseud. aeruginosa ATCC 27853	500	>1000	500	1000	500	>1000	500	1000
Enter. faecalis ATCC 29212	500	1000	250	500	1000	1000	500	1000
Staphyl. aureus ATCC 25923	500	1000	500	500	>1000	>1000	500	500
Sarcina lutea ATCC 9341	250	250	500	500	1000	1000	62.5	62.5
Lactobacillus rhamnosus	1000	>1000	500	>1000	>1000	>1000	1000	1000
Bifidobact. animalis subsp. lactis	500	1000	250	500	1000	1000	500	1000
Bacillus subtilis IP 5832	500	500	250	250	1000	>1000	250	500

MIC, minimum inhibitory concentration (μg/mL),
MBC, minimum bactericidal concentration (μg/mL)

Table 7. [4] Antibacterial activity of the ligands (**L15, L16**) and corresponding complexes (**C15,C16**).

[3] Radić et al., (2011b)
[4] Radić et al., (2011b)

The results of *in vitro* testing of antibacterial activities of the ligand (**L17**) and corresponding palladium(II) (**C17a**) and platinum(IV) (**C17b**) complexes are shown in Table 8.

Species	L17		C17a		C17b	
	MIC	MBC	MIC	MBC	MIC	MBC
Escherichia coli	>1000	>1000	250	500	>1000	>1000
Salmonella enterica	>1000	>1000	250	500	>1000	>1000
Pseud. aeruginosa ATCC 27853	250	>1000	15.63	500	125	500
Enter. faecalis ATCC 29212	500	>1000	31.25	500	250	500
Staphyl. aureus ATCC 25923	500	>1000	31.25	500	250	500
Sarcina lutea ATCC 9341	500	>1000	62.5	500	125	500
Lactobacillus rhamnosus	125	>1000	62.5	>1000	31.25	>1000
Bifidobact. animalis subsp. lactis	>1000	>1000	31.25	125	250	500
Bacillus subtilis IP 5832	500	>1000	250	500	250	500

MIC, minimum inhibitory concentration (μg/mL),
MBC, minimum microbiocidal concentration (μg/mL)

Table 8. [5]Antibacterial activity of the ligand (**L17**) and corresponding palladium(II) (**C17a**) and platinum(IV) (**C17b**) complexes.

The best activity manifested palladium(II) complex **C17a** with also the best seen result on *P. aeruginosa* ATCC 27853 (MIC 15.63 μg/mL). The same one at Gram-positive bacteria had MIC 31.25 – 62.5 μg/mL. Platinum (IV) complex **C17b** has weaker activity and the best result manifested on *L. rhamnosus* where MIC was 31.25 μg/mL (Radojević et al., 2011).

Species	L4		C4a		L18		C18	
	MIC	MBC	MIC	MBC	MIC	MBC	MIC	MBC
Escherichia coli	500	1000	1000	1000	>1000	>1000	>1000	>1000
Salmonella enterica	1000	>1000	1000	>1000	>1000	>1000	1000	>1000
Pseud. aeruginosa ATCC 27853	1000	1000	1000	>1000	1000	>1000	1000	>1000
Enter. faecalis ATCC 29212	500	500	1000	1000	500	1000	1000	1000
Staphyl. aureus ATCC 25923	500	500	500	1000	500	500	1000	1000
Sarcina lutea ATCC 9341	31.25	125	31.25	62.5	62.5	125	31.25	62.5
Lactobacillus rhamnosus	1000	1000	1000	1000	1000	1000	1000	1000
Bifidobact. animalis subsp. lactis	250	500	500	1000	500	500	1000	>1000
Bacillus subtilis IP 5832	125	500	500	1000	500	500	500	1000

MIC, minimum inhibitory concentration (μg/mL),
MBC, minimum microbiocidal concentration (μg/mL)

Table 9. [6]Antibacterial activity of the ligands (**L4, L18**) and corresponding complexes (**C4a, C18**).

Antibacterial activity of the tested platinum(IV) (**C4a, C18**) complexes and corresponding ligands (**L4, L18**) are shown in Table 9. Results for these testing was reported in the papers Stanković et al., (2011a,c). The ligands and corresponding platinum(IV) complexes demonstrated low antimicrobial activity. There was no difference in activities between the

[5] Radojević et al., (2011)
[6] Stanković et al., (2011a; 2011c)

ligands and corresponding complexes. The ligands and corresponding platinum(IV) complexes showed significant antibacterial activity against *S. lutea* ATTC 9341. MICs values were in range from 31.25 μg/mL to 62.5 μg/mL, and MBCs values were from 62.5 μg/mL to 125 μg/mL. The tested compounds did not affect the growth of Gram-negative bacteria or their activities were very low (MIC ranged from 500 μg/mL to >1000 μg/mL, MBC from 1000 μg/mL to >1000 μg/mL). Also, probiotic bacteria showed high resistance to the effects of tested substances. MICs were from 125 μg/mL to 1000 μg/mL, and MBCs were from 500 μg/mL to >1000 μg/mL (Stanković et al., 2011a,c).

The results of *in vitro* testing of antibacterial activities of the ligands (**L19, L20, L21**) and corresponding platinum(IV) (**C19, C20, C21**) complex are shown in Table 10.

Species	L19		C19		L20		C20		L21		C21	
	MIC	MBC	MIC	MBC	MIC	MBC	MIC	MBC	MIC	MBC	MIC	MBC
Escherichia coli	>1000	>1000	1000	>1000	>1000	>1000	1000	1000	>1000	>1000	1000	1000
Salmonella enterica	>1000	>1000	>1000	>1000	>1000	>1000	1000	1000	>1000	>1000	1000	1000
Pseud. aeruginosa ATCC 27853	>1000	>1000	1000	>1000	>1000	>1000	1000	>1000	>1000	>1000	1000	>1000
Enter. faecalis ATCC 29212	1000	>1000	1000	1000	1000	>1000	250	500	1000	1000	125	500
Staphyl. aureus ATCC 25923	1000	>1000	500	1000	1000	>1000	250	250	1000	>1000	125	250
Sarcina lutea ATCC 9341	1000	>1000	7.81	15.625	1000	>1000	15.625	31.25	1000	>1000	31.25	62.5
Lactobacillus rhamnosus	>1000	>1000	>1000	>1000	>1000	>1000	>1000	>1000	>1000	>1000	>1000	>1000
Bifidobact. animalis subsp. lactis	125	250	1000	1000	<31.25	125	500	500	<31.25	250	125	500
Bacillus subtilis IP 5832	125	250	250	1000	250	250	250	250	250	250	125	250

MIC, minimum inhibitory concentration (μg/mL),
MBC, minimum microbiocidal concentration (μg/mL)

Table 10. Antibacterial activity of the ligands (**L19, L20, L21**) and corresponding complexes (**C19, C20, C21**).

The difference in action between ligands and corresponding complexes can be seen at Gram-positive bacteria. Ligands have significant antimicrobial effect on probiotic bacteria (**L20**, **L21**), and complexes on Gram-positive bacteria (**C19, C20, C21**). **C21** has better antimicrobial effect than two other complexes. The lowest antimicrobial action of compounds was on Gram-negative bacteria, where tested concentrations of ligands almost didn't have the influence, while corresponding complexes had some better action, but still weak and limited. *L. rhamnosus* also showed similar resistance to the action of tested compounds (none of the tested concentrations had the influence on its growth), while the other probiotic bacteria were more sensitive, especially to the action of ligands, where MIC goes from <31.25 μg/mL to 250 μg/mL. At complexes MIC is in the range from125 μg/mL to 1000 μg/mL.

The gram-positive bacteria were more sensitive than the gram-negative bacteria. The platinum(IV) complexes showed high antibacterial activity against Gram-positive bacteria. MIC values were in range from 7.81 μg/mL to 1000 μg/mL, and MBC values were from 15.63 μg/mL to 1000 μg/mL depending on the species of bacteria. The most sensitive was *S. lutea* ATCC 9341 (MIC values are 7.81 μg/mL, 15.625 μg/mL and 31.25 μg/mL for different complexes.

Species	Doxycycline	
	MIC	MBC
Escherichia coli	7.81	15.625
Salmonella enterica	15.625	31.25
Pseud. aeruginosa ATCC 27853	62.5	125
Enter. faecalis ATCC 29212	7.81	62.5
Staphyl. aureus ATCC 25923	0.224	3.75
Sarcina lutea ATCC 9341	< 0.448	7.81
Lactobacillus rhamnosus	7.81	31.25
Bifidobact. animalis subsp. lactis	31.25	62.5
Bacillus subtilis IP 5832	1.953	15.625

MIC, minimum inhibitory concentration (μg/mL),
MBC, minimum microbiocidal concentration (μg/mL)

Table 11. Antibacterial activity of the positive control - doxycycline

In general, the ligands demonstrated low and selective antimicrobial activity (with few exceptions) and the complexes showed selective and moderate antibacterial activity. MIC values were in range from <7.81μg/mL to >1000 μg/mL and MBC values from 15.625 μg/mL to >1000 μg/mL depending on the species of bacteria. The Gram-positive bacteria were more sensitive than the Gram-negative bacteria. The most sensitive species is *S. lutea* ATCC 9341. Tested probiotics, with a few exceptions, indicate high resistance toward tested compounds. *L. rhamnosus* shows the highest resistance among them. The tested complexes **C1**, **C2**, **C3** and **C17a** exhibit strong activity towards *E. coli*, *P. aeruginosa* ATCC 27853 and *E. faecalis* ATCC 29212. The **L6**, **L7** and **C6**, **C7** exhibit strong antibacterial activity towards *E. coli*. The tested compounds did not affect *S. enterica* or their activities were low. Some activity showed palladium(II) complexes (**C1, C2 , C3, C6** and **C17a**). At the ligands the most effective antimicrobial activity show **L6, L7, L9, L10** and **L11** while the most active complexes are **C1, C2, C3, C6** and **C17a.** For eleven ligands (**L1** - **L11**) and corresponding palladium(II) complexes (**C1** - **C11**) antifungal activity is investigated. Palladium(II) complexes showed good antifungal activity opposite to ligands. This study are in keeping with our research to a great extent (Radojević et al., 2010).

4. Conclusion

The intensity of antimicrobial action varied depending on the species of microorganism and on the type of tested compounds. The tested ligands, with few exceptions, show low antimicrobial activity. The difference between antimicrobial activity of the ligands and corresponding palladium(II) and platinum(IV) complexes is noticed and, in general, the most active were palladium(II) complexes. The Gram-positive bacteria were more sensitive than the Gram-negative bacteria. The most sensitive species is *Sarcina lutea* ATCC 9341 and the most resistant is *Salmonella enterica* where the tested compounds did not affect or their activities were low. Tested probiotics, with a few exceptions, also indicate high resistance toward tested compounds.

5. Acknowledgement

The authors are grateful for financial support to the Ministry of Education and Science of Republic of Serbia (projects No. OI172016 and III41010).

6. References

Agarwal, S.K. (2007). Synthesis & Characterization of Some Mixed Ligand Complexes of Pd(II), Rh(III) and Pt(IV) with Carboxylic Hydrazones as Primary and Dithiooxamide as Co-ligand. *Asian Journal of Chemistry*, Vol.19, No.4, pp. 2581-2585, ISSN: 0970-7077

Aghatabay, N. M.; Somer, M.; Senel, M.; Dulger, B. & Gucin, F. (2007). Raman, FT-IR, NMR spectroscopic data and antimicrobial activity of bis[μ_2-(benzimidazol-2-yl)-2-ethanethiolato-*N*,*S*,*S*-chloro-palladium(II)] dimer, $[(\mu_2\text{-}CH_2CH_2NHNCC_6H_4)PdCl]_2$ C_2H_5OH complex. *European Journal of Medicinal Chemistry*, Vol.42, No.8, (August 2007), pp. 1069-1075, ISSN: 0223-5234

Ali, A.M., Mirza, A.H., Butcher, R.J. & Crouse, K.A. (2006). The preparation, characterization and biological activity of palladium(II) and platinum(II) complexes of tridentate NNS ligands derived from S-methyl- and S-benzyldithiocarbazates and the X-ray crystal structure of the [Pd(mpasme)Cl] complex. *Transition Metal Chemistry,* Vol.31, No.1, (February 2006), pp. 79-87, Print ISSN: 0340-4285, Online ISSN: 1572-901X

Al-Hazmi, G.A., El-Metwally, N.M., El-Gammal, O.A. & El-Asmy, A.A. (2008). Synthesis, spectral characterization and eukaryotic DNA degradation of thiosemicarbazones and their platinum(IV) complexes. *Spectrochimica Acta*, Part A: *Molecular and Biomolecular Spectroscopy,* Vol.69, No.1, (January 2008), pp. 56-61, ISSN: 1386-1425

Andrews, J.M. (2005). BSAC standardized disc susceptibility testing method (version 4). *Journal of Antimicrobial Chemotherapy*, Vol.56, No.1, (July 2005), pp. 60-76, Print ISSN 0305-7453, Online ISSN 1460-2091

Banfi E., Scialino G. & Monti-Bragadin C. (2003). Development of a microdilution method to evaluate Mycobacterium tuberculosis drug susceptibility. *Journal of Antimicrobial Chemotherapy,* Vol.52, No.5, (*November 2003*), pp. 796-800, Print ISSN 0305-7453, Online ISSN 1460-2091

Biyala, M.K., Sharma, K., Swami, M., Fahmi, N. & Vir Singh, R. (2008). Spectral and biocidal studies of palladium(II) and platinum(II) complexes with monobasic bidentate Schiff bases. *Transition Metal Chemistry,* Vol.33, No.3, (April 2008), pp. 377 – 381, Print ISSN: 0340-4285, Online ISSN: 1572-901X

Brudzinska, I., Mikata, Y., Obata, M., Ohtsuki, C. & Yano, S. (2004). Synthesis, structural characterization, and antitumor activity of palladium(II) complexes containing a sugar unit. *Bioorganic & Medicinal Chemistry Letters*, Vol.14, No.10, (17 May), pp. 2533–2536, ISSN: 0960-894X

Coombs, R.R., Ringer, M.K., Blacquiere, J.M., Smith, J.C., Neilsen, J.S., Uh, Y., Gilbert, J.B., Leger, L.J., Zhang, H., Irving A.M., Wheaton, S.L., Vogels, C.M., Westcott, S.A., Decken, A. & Baerlocher, F.J. (2005). Palladium(II) Schiff base complexes derived

from sulfanilamides and aminobenzothiazoles. *Transition Metal Chemistry,* Vol.30, No.4, (May 2005), pp. 411-418, Print ISSN: 0340-4285, Online ISSN: 1572-901X

Dimitrijević, D.P., Vujić, J.M., Garcia-Granda, S., Menendez-Taboada, L. & Trifunović S.R. (2010). Synthesis and crystal structure of O,O'-dipropyl-ethylenediamine-N,N'-di-(S,S)-(2,2'-dibenzyl)-acetate dihydrochloride. *Proceedings of XVII Conference of the Serbian Crystallographic Society,* pp. 48, ISBN: 978-86- 6009-004-3, Ivanjica, Serbia, June 3-5, 2010.

Dimitrijević, D.P., Radić G.P., Glođović, V.V., Radojević I.D., Stefanović O.D. , Čomić Lj., Ratković Z.R., Valkonen A., Rissanen, K. & Trifunović, S. R. (2011). Crystal structure of bis-(S-benzyl-thiosalicylate)-palladium(II) complex, $[Pd(S\text{-}bz\text{-}eddp)_2]$. *Proceedings of XVIII Conference of the Serbian Crystallographic Society,* pp. 44, ISBN: 978-86-7031-194-7, Fruška Gora, Serbia, June 2-4, 2011.

Kizilcikli, I., Kurt, Y.D., Akkurt, B., Genel, A.Y., Birteksöz, S., Ötük, G. & Ülküseven, B. (2007). Antimicrobial Activity of a Series of Thiosemicarbazones and Their ZnII and PdII Complexes. *Folia Microbiologica*, Vol.52, No.1, (January 2007), pp. 15-25, Print ISSN: 0015-5632, Online ISSN: 1874-9356

Kovala-Demertzi, D., Demertzis, M.A., Miller, J.R., Papadopoulou, C., Dodorou, C. & Filousis, G. (2001). Platinum(II) complexes with 2-acetyl pyridine thiosemicarbazone: Synthesis, crystal structure, spectral properties, antimicrobial and antitumour activity, *Journal of Inorganic Biochemistry,* Vol.86, No.2-3, (September 2001), pp. 555-563, ISSN: 0162-0134

Garoufis, A., Hadjikakou, S.K. & Hadjiliadis, N. (2009). Palladium coordination compounds as anti-viral, anti-fungal, anti-microbial and anti-tumor agents. *Coordination Chemistry Reviews,* Vol.253, No.9-10, (May 2009), pp. 1384–1397, ISSN: 0010-8545

Guerra W., de Andrade Azevedo E., de Souza Monteiro A. R., Bucciarelli-Rodriguez M., Chartone-Souza E., Nascimento A. M. A., Fontes A. P. S., Le Moyec L., Pereira-Maia E. C. (2005). Synthesis, characterization, and antibacterial activity of three palladium(II) complexes of tetracyclines. *Journal of Inorganic Biochemistry,* Vol.99, No.12, (December 2005), pp. 2348–2354, ISSN: 0162-0134

Fluit, A.C., Jones, M.E., Schmitz, F.J., Acar, J., Gupta, R., Verhoef, J., & the SENTRY Participants Group. (2000). Antimicrobial susceptibility and frequency of occurrence of clinical blood isolates in Europe from the SENTRY Antimicrobial Surveillance Program, 1997 and 1998. *Clinical Infectious Diseases,* Vol.30, No.3, (March 2000), pp. 454-460, ISSN: 1058-4838

Manav, N., Mishra, A.K. & Kaushik, N. K. (2006). In vitro antitumour and antibacterial studies of some Pt(IV) dithiocarbamate complexes. *Spectrochimica Acta*, Part A: *Molecular and Biomolecular Spectroscopy.* Vol.65, No.1, (September 2006), pp. 32-*35*, ISSN: 1386-1425

Mishra, A.K. & Kaushik, N.K. (2007). Synthesis, characterization, cytotoxicity, antibacterial and antifungal evaluation of some new platinum (IV) and palladium (II) complexes of thiodiamines. *European Journal of Medicinal Chemistry*, Vol.42, No.10, (October 2007), pp. 1239-1246, ISSN: 0223-5234

Mishra A.K., Mishra, S.B., Manav, N. & Kaushik, N.K. (2007a). Platinum(IV) and palladium(II) thiosemicarbazide and thiodiamine complexes: A spectral and antibacterial study. *Journal of Coordination Chemistry*. Vol.60, No.18, (September 2007) pp. 1923-1932, Print ISSN: 0095-8972, Online ISSN: 1029-0389

Mishra, A.K., Mishra, S.B., Manav, N., Kumar, R., Sharad, R., Chandra, R., Saluja, D. & Kaushik, N.K. (2007b). Platinum (IV) thiohydrazide, thiodiamine and thiohydrazone complexes: A spectral, antibacterial and cytotoxic study. *Spectrochimica Acta* Part A: *Molecular and Biomolecular Spectroscopy*, Vol.66, No.4-5, (April 2007), pp. 1042-1047, ISSN: 1386-1425

Radić, G.P., Glođović, V.V., Garsia-Granda, S., Menéndez-Taboada, L., Ratković, Z.& Trifunović S.R. (2010a). Crystal structure of 1,2-diphenyl-ethylenediamine- N,N'-di-3- propanoic acid dihydrochloride. *Proceedings of XVII Conference of the Serbian Crystallographic Society*, pp. 36, ISBN: 978-86- 6009-004-3, Ivanjica, Serbia, June 3-5, 2010.

Radić, G.P., Glođović, V.V., Heinemann, F.W. & Trifunović, S.R. (2010b). Synthesis and crystal structure of palladium(II) complex with O,O'-diethyl- (S,S)-ethylenediamine-N,N'-di-2-(3-methyl) butanoate. *Proceedings of XVII Conference of the Serbian Crystallographic Society*, pp. 60, ISBN: 978-86-6009-004-3, Ivanjica, Serbia, June 3-5, 2010.

Radić, G.P., Glođović, V.V., Kaluđerović, G.N., Heinemann, F.W. & Trifunović, S. R. (2011a). Palladium(II) complexes with R_2edda derived ligands. Part V. Reaction of O,O'-Diethyl-(S,S)-ethylenediamine-N,N'-di-2-(3-methyl)butanoate with $K_2[PdCl_4]$. *Transition Metal Chemistry,* Vol.36, No.4 , (May 2011), pp. 331–336, ISSN: 0340-4285

Radić, G.P., Glođović, V.V., Radojević, I.D., Stefanović, O.D., Čomić, Lj.R., Ratković, Z.R., Valkonen, A., Rissanen, K. & Trifunović, S.R. (2011b). Synthesis, characterization and antimicrobial activity of palladium(II) complexes with some alkyl derivates of thiosalicylic acids. Crystal structure of *bis*(S-benzyl-thiosalicylate)-palladium(II) complex, $[Pd(S\text{-}bz\text{-}thiosal)_2]$. *Polyhedron,* Accepted, In Press, n.d. ISSN: 0277-5387

Radojević, I., Čomić, Lj., Stefanović, O., Glodjović, V., Vasić, V., Vujić, J. & Trifunović, S. (2010). Antimicrobial activity ligands and their corresponding palladium(II) complexes against Aspergillus species. *Proceedings of ICAR* 2010, *International Conference on Antimicrobial Research,* pp. 475-476, Available from: http://www.formatex.org/icar2010/index.html, Valladolid, Spain, November 3-5, 2010.

Radojević, I., Stefanović, O., Radić, G., Glođović, V., Čomić, Lj. & Trifunović, S. (2011). *In vitro* antimicrobial activity of novel platinum(iv) and palladium(ii) complexes with 1,2-diphenyl-ethylenediamine-n,n'-di-3-propanoic acid. *Proceedings of Preclinical testing of active substances and cancer research*, *with International Symposium on Anti-Cancer Agents, Cardiotoxicity and Neurotoxicity,* pp. 10-11, ISBN: 978-86-7760-064-8, Kragujevac, Serbia, March 16-18, 2011.

Sarker, S.D., Nahar, L. & Kumarasamy, Y. (2007). Microtitre plate-based antibacterial assay incorporating resazurin as an indicator of cell growth, and its application in the in vitro antibacterial screening of phytochemicals. *Methods,* Vol.42, No.4, (August 2007), pp. 321-324,. ISSN: 1046-2023

Stanković, M., Radić, G., Glođović, V., Radojević, I., Stefanović, O., Čomić, Lj. & Trifunović, S. (2011a). Antimicrobial activity of ethyl esters of (*S,S*)-ethylenediamine-*N,N'*-di-2-propanoic and (*S,S*)- ethylenediamine-*N,N'*-di-2-(3-methyl)-butanoic acids and corresponding platinum(IV) complexes. *Proceedings of Preclinical testing of active substances and cancer research, with International Symposium on Anti-Cancer Agents, Cardiotoxicity and Neurotoxicity,* pp. 9-10, ISBN: 978-86-7760-064-8, Kragujevac, Serbia, March 16-18, 2011.

Stanković, M.Z., Radić, G.P., Glođović, V.V., Klisurić, O.R. & Trifunović, S.R. (2011b). Synthesis and crystal structure of tetrachoride-(O,O'-diethyl-(S,S)-ethylenediamine-N,N'-di-2-propanoato)-platinum(IV). *Proceedings of XVIII Conference of the Serbian Crystallographic Society*, pp. 42, ISBN: 978-86-7031-194-7, Fruška Gora, Serbia, June 2-4, 2011.

Stanković, M.Z., Radić, G.P., Glođović, V.V., Radojević, I.D., Stefanović, O.D., Čomić, L.R., Klisurić, O.R., Djinović, V.M. & Trifunović, S.R., (2011c). Stereospecific ligands and their complexes IX: Synthesis, characterization and antimicrobial activity of ethyl esters of (S,S)-ethylenediamine-N,N'-di-2-propanoic and (S,S)-ethylenediamine-N,N'-di-2-(3-methyl)-butanoic acids and corresponding platinum(IV) complexes: Crystal structure of tetrachloride-(O,O'-diethyl-(S,S)-ethylenediamine-N,N'-di-2-propanoato)-platinum(IV), [PtCl4(det-S,S-eddp)]. *Polyhedron*, In Press, doi: 10.1016/j.poly.2011.05.034, ISSN: 0277-5387

Vasić, G., Glodjović, V., Radojević, I., Stefanović, O., Čomić, Lj. & Trifunović, S. (2010). Stereospecific ligands and their complexes. V. Synthesis, characterization and antimicrobial activity of palladium (II) complexes with some alkyl esters of ethylenediamine-*N,N'*-di-*S,S*-2-propionic acid. *Inorganica Chimica Acta*, Vol.363, No.13, (October 2010), pp. 3606-3610, ISSN: 0020-1693

Vieira, L.M.M., de Almeida, M.V., Lourenço, M.C.S., Bezerra, F.A.F.M. & Fontes, A.P.S. (2009). Synthesis and antitubercular activity of palladium and platinum complexes with fluoroquinolones. *European Journal of Medicinal Chemistry*, Vol.44, No.10, (October 2009), pp. 4107- 4111, ISSN: 0223-5234

Vujić, J.M., Cvijović, M., Kaluđerović, G.N., Milovanović, M., Zmejkovski B.B., Volarević V., Arsenijević N., Sabo, T.J. & Trifunović, S.R. (2010). Palladium(II) complexes with R_2edda derived ligands. Part IV. *O,O'*-dialkyl esters of (*S,S*)-ethylenediamine-*N,N'*-di-2-(4-methyl)-pentanoic acid dihydrochloride and their palladium(II) complexes: Synthesis, characterization and *in vitro* antitumoral activity against chronic lymphocytic leukemia (CLL) cells. *European Journal of Medicinal Chemistry,* Vol.45, No.9, (September 2010), pp. 3601-3606, ISSN: 0223-5234

Vujić, J.M., Garcia-Granda, S., Menendez-Taboada, L. & Trifunović, S.R. (2011). Crystal structure of palladium(II) complex with *O,O'*- dipentil-etilenediamine- *N,N'*-di-(*S,S*)-2(4-methy)-pentanoate ligand. *Proceedings of XVIII Conference of the Serbian Crystallographic Society*, pp. 40, ISBN: 978-86-7031-194-7, Fruška Gora, Serbia, June 2-4, 2011.

IntechOpen

IntechOpen

© 2012 The Author(s). Licensee IntechOpen. This is an open access article distributed under the terms of the Creative Commons Attribution 3.0 License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

IntechOpen

IntechOpen