Synthesis, characterization and crystal structures of platinum(II) saccharinate complexes with 1,5-cyclooctadiene

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Abstract: Two new platinum(II) complexes, namely [PtCl(sac)(COD)] (1) and [Pt(sac)_2(COD)] (2) (sac = saccharinate and COD = 1,5-cyclooctadiene), were synthesized and characterized by elemental analysis, IR, NMR, ESI-MS spectroscopic and thermal analysis (TG/DTA) methods. The platinum(II) complexes were prepared from the reaction of [PtCl_2(COD)] with Na(sac)•2H_2O. The addition of the sac ligand resulted in the replacement of 1 and 2 chlorido ligands in [PtCl_2(COD)] to yield 1 and 2, respectively. The structures of the complexes were determined by single crystal X-ray diffraction and showed a distorted square planar coordination geometry around platinum(II). COD acted as a π-donor ligand, while sac was N-coordinated in both complexes. The TG/DTA data indicated that both complexes were thermally stable up to 220 °C in air and their thermal decompositions yielded Pt as a final product. Complexes 1 and 2 were also designed as possible precursors to synthesize new mixed-ligand platinum(II) sac complexes in a one-pot reaction.

Key words: Pt(II) complex, saccharinate, 1,5-cyclooctadiene, crystal structure

1. Introduction
After the discovery of the cell growth inhibition effect of cisplatin by Rosenberg [1–3], the design and synthesis of new platinum(II) complexes received increasing attention. For this purpose, several synthetic routes were used. One way is to synthesize precursors to prepare new platinum(II) complexes. The reaction of a simple platinum(II) complex (K_2[PtCl_4]) with the mono-, di- or tridentate ligands usually leads to the formation of chloroplutinum(II) complexes bearing these ligands. In a subsequent reaction, the chlorido ligands in the precursor can be exchanged by another ligand to yield the desired platinum(II) complex. Another alternative way is to use [PtCl_2(COD)] (COD = 1,5-cyclooctadiene), which serves as an excellent starting complex for a wide range of organoplatinum(II) compounds [4]. The chlorido ligands in [PtCl_2(COD)] can be replaced by other higher halides (Br^- or I^-) or anionic organic ligands due to the high π trans effect of COD [5]. Organoplatinum(II) complexes [Pt(R)(L)(COD)] (R = organic groups such as alkyl, aryl or alkynyl; L = other ligands) received great interest and were widely used in catalysis [6–10], material science [11,12] and medicinal research as anticancer agents [13–19].

The artificial sweetener saccharin (sacH, 1,1-dioxo-1,2-benzothiazol-3-one) loses its imine hydrogen in solution and the corresponding saccharinate (sac) anion acts as a multifunctional ligand towards various metal
ions [20]. It forms coordination compounds from mononuclear to polynuclear. Among the metal complexes of sac, the platinum(II) complexes of sac with different ligands particularly seem to be promising anticancer agents [21–29]. In the synthesis of these complexes, a variety of synthetic strategies was applied. One efficient route was the progressive replacement of the chlorido ligands in [PtCl₂(COD)] by the sac ligand to obtain the first examples of organometallic platinum(II) sac complexes, [PtCl(sac)(COD)] (1), and [Pt(sac)₂(COD)] (2).

In this study, the synthesis, characterization and crystal structures of 1 and 2 were described. Both complexes can also be used as precursors for the preparation of new platinum(II) sac complexes. The COD ligand in 1 and 2 can further be exchanged by σ-donor neutral ligands to give novel mixed-ligand chlorido platinum(II) sac or bis(sac)platinum(II) complexes. The synthetic method seems to be an attractive alternative way to synthesize new platinum(II) sac complexes, because it may be regarded as a one-pot reaction with high yields. However, the other procedures include multistep synthesis and usually result in low yields.

2. Results and discussion

2.1. Synthesis and characterization

[PtCl(sac)(COD)] (1) and [Pt(sac)₂(COD)] (2) were designed as starting materials for the synthesis of new mixed-ligand platinum(II) complexes of sac. 1 and 2 were synthesized by the reaction of [PtCl₂(COD)] with Na(sac)•2H₂O in a molar ratio of 1:2 and 1:5, respectively. Both complexes were obtained in high yields over 90%. They are stable in air at room temperature (rt) and soluble in MeCN, MeOH, EtOH, DMSO, and DMF as well as in the aqueous solutions of these solvents. The conductivity measurements at rt indicated that both complexes are nonelectrolyte in MeOH.

The structures of 1 and 2 were confirmed by a number of spectroscopic methods. The IR spectra of the complexes present the characteristic absorption bands of both COD and sac ligands. The weak bands centred at 3008 and 3077 cm⁻¹ are assigned to the C=CH vibrations of COD and sac, respectively, while the aliphatic CH bands of COD occur between 2919 and 2962 cm⁻¹. The strong bands at 1673 and 1691 cm⁻¹ are attributed to the carbonyl group of sac in 1 and 2, respectively. The asymmetric and symmetric stretching of the sulfonyl group of sac appear as very sharp bands at ca. 1302/1285 and 1172/1155 cm⁻¹, respectively. Moreover, the weak band centred at 1335 cm⁻¹ is due to the symmetric vibration of the CNS moiety of sac and the asymmetric mode of this group is observed at ca. 970 cm⁻¹ as a strong band.

The ¹H NMR spectra in Figure 1 display the phenyl protons of sac in the range of 7.94–7.73 ppm. The 2=CH protons of COD in 1 appear as 2 signals at 5.84 and 5.08 ppm, while those in 2 occur at 5.52 ppm. The notable difference between the 2 olefinic chemical shifts in 1 is due to the trans influence of the chlorido and sac ligands. On the other hand, a COD ligand together with 2 sac ligands in 2 results in only 1 signal for the 2 equivalent =CH protons. The splitting of these signals is evident because of coupling with the Pt nucleus. The Jₚₜ,H(=CH, COD) coupling constants are found as 36 and 64 Hz for 1 and consistent with the somewhat higher trans influence of sac [15,29]. The corresponding coupling constant is approximately 40 Hz for 2. In addition, the signals between 2.78 and 2.08 ppm are assigned to the methylene protons of COD. The ¹³C{¹H}NMR spectra of both complexes exhibit the expected number of signals. The carbonyl signal of sac appears at 159.1 and 158.9 ppm for 1 and 2, respectively. The phenyl C atoms are observed in the range of 141.7–121.4 ppm for 1, and 141.7–121.0 ppm for 2. Complex 1 gives rise to 2 olefinic C signals at 106.2 and 101.8 ppm and 2 methylene C signals at 30.7 and 27.8 ppm, while the corresponding C atoms in 2 resonance at 106.1 ppm and 30.4 ppm.
The ionization of the complexes in MeOH was investigated by electrospray mass spectroscopy. The positive ion electrospray ionization (ESI$^+$) mass spectra of 1 present the following ions [M + 1]$^+$ (22%; $m/z = 522.2$), [Pt(sac)(MeOH)]$^+$ (100%; $m/z = 408.4$) and [Pt(sac)]$^+$ (32%; $m/z = 375.5$), while 2 forms [M + Na]$^+$ (39%; $m/z = 691.4$), [Pt(sac)(MeOH)]$^+$ (63%; $m/z = 408.4$) and [Pt(sac)]$^+$ (100%; $m/z = 375.5$) ions in solution under the experimental conditions. The molecular ion peaks of 1 and 2 are apparent in the spectra as the [M + 1]$^+$ ion ($m/z 522.2$) and the sodium adduct, [M + Na]$^+$ ($m/z 691.4$), respectively, while the base peaks (100%) correspond to the [Pt(sac)(MeOH)]$^+$ ion at $m/z 408.4$, and the [Pt(sac)]$^+$ ion at $m/z 375.5$ in the spectra of 1 and 2, respectively.

![NMR Spectra](image)

**Figure 1.** $^1$H and $^{13}$C($^1$H)NMR spectra of 1 (a) and 2 (b).

### 3. Structures of the platinum(II) complexes

Slow evaporation of the saturated solutions of 1 and 2 at rt afforded white prisms. Complexes 1 and 2 crystallize in the monoclinic space group $P2_1/c$ and orthorhombic space group $Pna2_1$, respectively. The molecular structures of both complexes were given in Figure 2, while selected bond lengths and angles are given in Table 1. In both complexes, the platinum(II) ion shows a distorted square planar coordination geometry defined by the mid-points of the 2 $\pi$-coordinated double bonds of COD, 1 chloride and 1 $N$-bonded sac anion in 1, and 2 $N$-coordinated sac ligands in 2 (Figure 2). In 1 and 2, the COD ligand coordinates to the platinum(II) ion in $\eta^4$-type coordination and in the boat conformation with the double-bond lengths of ca. 1.38 Å. The Pt–C
bond distances lie within the typical range for the platinum(II) complexes of COD [17,30,31]. However, 2 sets of the Pt–C bonds were observed in 1, most likely due to the different trans influences of the chlorido and sac ligands. In addition, 1 of the 4 Pt–C bonds in 2 is notably shorter than the rest and consequently, the molecule retains a pseudo C2 symmetry in the solid state. This is consistent with the similar observations reported for [Pt(COD)Me2] [32]. The sac ligand is coordinated to platinum(II) through the negatively charged N atom. The 2 sac ligands in 2 are oriented almost perpendicularly with a dihedral angle of 86.15(6)° to reduce the steric hindrance. The Pt–N bond distances in both complexes are similar and compare well with the corresponding bonds in the platinum(II) complexes with sac [22–29,33]. On the other hand, the Pt–Cl bond distance of 2.301(2) Å in 1 is somewhat shorter than those in cis-[PtCl(sac)(L)2] [26,29,33] and [PtCl(COD)Me] [32].

The discrete molecules of 1 and 2 are held together in the solid state by a number of weak C–H•••O hydrogen bonds involving the carbonyl or sulfonyl oxygen atoms of sac. Interestingly, no Cl•••H interactions are observed in 1.

Figure 2. Molecular structures of 1 and 2. Hydrogen atoms were omitted for clarity.

4. Thermal analysis
The thermal stability and decomposition behaviour of the complexes were studied by TG and DTA in air. As shown in Figure 3, complexes 1 and 2 are thermally stable up to ca. 220 °C. 1 decomposes in 2 steps, which do not correspond to the removal of any species. Its DTA curve presents a small endothermic and a highly exothermic effects centred at 250 and 340 °C, respectively. The latter is likely to due to combustion of the sac moiety. The decomposition of this complex ends at 360 °C to give metallic Pt as a residue (found: 36.2% and calcd: 37.5%). On the other hand, complex 2 also exhibits a 2-stage exothermic decomposition centred at 253 and 331 °C in the DTA curve. The decomposition of 2 also yields metallic Pt as an end product (found: 30.6% and calcd: 29.2%) at 390 °C.
Table 1. Selected bond lengths (Å) and bond angles (°) of 1 and 2.

|       | 1     | 2     |
|-------|-------|-------|
| Pt–Cl1 | 2.301(2) | -     |
| Pt–N1  | 2.041(4) | 2.054(14) |
| Pt–N2  | -     | 2.006(14) |
| Pt–C1  | 2.142(6) | 2.177(18) |
| Pt–C2  | 2.158(6) | 2.180(20) |
| Pt–C5  | 2.172(4) | 2.173(17) |
| Pt–C6  | 2.182(4) | 2.134(19) |
| Pt–X1\(^a\) | 2.033 | 2.071 |
| Pt–X2\(^a\) | 2.062 | 2.039 |
| N1–Pt–C11 | 89.89(13) | - |
| N1–Pt–N2  | -     | 90.4(6) |
| N1–Pt–C1  | 90.00(19) | 91.8(6) |
| N1–Pt–C2  | 92.76(18) | 92.6(7) |
| N1–Pt–C5  | 158.73(15) | 165.7(9) |
| N1–Pt–C6  | 163.82(16) | 156.9(8) |
| N2–Pt–C1  | -     | 166.5(8) |
| N2–Pt–C2  | -     | 156.8(7) |
| N2–Pt–C5  | -     | 91.2(7) |
| N2–Pt–C6  | -     | 89.4(7) |
| Cl1–Pt–C1 | 158.06(14) | - |
| Cl1–Pt–C2 | 163.93(14) | - |
| Cl1–Pt–C5 | 90.51(16) | - |
| Cl1–Pt–C6 | 92.54(17) | - |
| C1–Pt–C5 | 97.4(2)  | 89.9(7) |
| C1–Pt–C6 | 81.8(2)  | 83.3(7) |
| C2–Pt–C5 | 81.3(2)  | 80.4(7) |
| C2–Pt–C6 | 89.3(2)  | 96.6(7) |

\(^a\) X1 and X2 refer to the centroids in the middle of olefinic bonds C1–C2, and C5–C6, respectively.

5. Conclusions

Two new platinum(II) complexes containing COD and sac ligands were successfully synthesized via the progressive replacement of the chloride ligands in [PtCl₂(COD)] by the sac ligand. Both complexes were characterized by spectroscopic (IR, NMR and ESI-MS) and thermal methods (TG/DTA). Their crystal and molecular structures were determined using X-ray crystallography. The platinum(II) ion in both complexes has a distorted square-planar coordination geometry mainly due to coordination of the chelating COD ligand. [Pt(sac)₂(COD)]\(^2\) has approximate \(C_2\) symmetry, which results in a signal for the olefinic proton and carbon atoms in \(^1\)H and \(^{13}\)C spectra, whereas [PtCl(sac)(COD)]\(^1\) gives 2 signals in the NMR spectra for the corresponding groups due to the difference in the trans effects of the chlorido and sac ligands. The complexes exhibit high thermal
stability in air. Finally, both complexes can be considered as precursors for the synthesis of new mixed-ligand platinum(II) sac in a one-pot reaction, in which COD in the complexes is readily replaced by the other ligands.

6. Experimental

6.1. Materials and measurements

[PtCl\(_2\)(COD)] was prepared according to the reported methods [4]. Elemental analyses for C, H, and N were performed using a Costech elemental analyser. FTIR spectra were recorded on a Perkin Elmer Spectrum Two FT-IR spectrophotometer in the frequency range 4000-400 cm\(^{-1}\). NMR spectra were obtained using a Bruker Avance III (400.13 MHz \(^1\)H and 100.62 MHz \(^{13}\)C) NMR spectrometer in DMSO-\(d_6\). ESI-MS spectra were recorded using a Bruker Daltonics Microtof II-ESI-TOF mass spectrometer. Thermal analysis curves (TG and DTA) were obtained from a Seiko Exstar TG/DTA 6200 thermal analyser in a flowing atmosphere of air with a heating rate of 10 K min\(^{-1}\) using a sample size of ca. 10 mg and platinum crucibles. The electrical conductivity measurements of the complexes in MeOH were carried out with HANNA HI 5521 at rt. Melting points are measured using a BUCHI 560 instrument.

6.2. Synthesis of the platinum(II) complexes

6.2.1. Synthesis of [PtCl(sac)(COD)] (1)

A solution of [PtCl\(_2\)(COD)] (0.25 mmol, 94 mg) in CH\(_2\)Cl\(_2\) (10 mL) was added to a solution of Na(sac)•2H\(_2\)O (0.50 mmol, 121 mg) in MeOH (20 mL). The resulting solution was refluxed at 70 °C for 24 h and then the solvent was removed using a rotary evaporator to yield a white powder. The powder was washed with water twice and dried in air. Single crystals of the complex were obtained by slow crystallization from a mixture of EtOH/H\(_2\)O/DMF within 4 weeks at rt.

[PtCl(sac)(COD)] (1). White powder. Yield: 117 mg (90%). Mp: 246-251 °C (decomp.). Anal. calcd. for C\(_{15}\)H\(_{16}\)ClNO\(_3\)PtS: C, 34.59; H, 3.10; N, 2.69%. Found C, 34.92; H, 3.27; N, 2.48%. IR (\(\nu\)/cm\(^{-1}\)): 3076w, 3025w (C=CH), 2962w, 2927w (CH\(_2\)), 1673s (C=O), 1593w, 1458w, 1418w (C=C), 1333w \(\nu_s\) (CNS), 1303vs,
Crystallographic Data and Refinement Parameters of [Pt(sac)]

The complex was prepared using a similar method explained for [PtCl₂(COD)/Na(sac)]. ESI–MS (m/z): 696.5 (19%, calcd. 696.6) [Pt(sac)₂(MeCN)₂(MeOH) + Na]⁺, 598.0 (49%, calcd. 598.1) [Pt(sac)(COD)(MeOH) + Na]⁺, 522.2 (22%, calcd. 521.9) [M + 1]⁺, 408.4 (100%, calcd. 408.9) [Pt(sac)(MeOH)]⁺, 375.5 (32%, calcd. 376.0) [Pt(sac)]⁺, 339.1 (18%, calcd. 334.1) [Pt(COD)(MeOH) − H]⁺.

6.2.2 Synthesis of [Pt(sac)(COD)] (2)
The complex was prepared using a similar method explained for 1. The [PtCl₂(COD)]/Na(sac) • 2H₂O ratio was 1/5 in this case. The complex was crystallized from a mixture of EtOH/H₂O/DMSO after 4 weeks at rt.

6.3 X-ray crystallography

The intensity data of the platinum(II) complexes were collected on a Rigaku Xcalibur X-ray diffractometer with EOS CCD detector using Mo-Kα radiation (0.71073 Å) with ω-scan mode. The structures were solved by direct methods using SHELXTL [34], and refined by a full-matrix least-squares minimization with SHELXL [35], using Olex2 [36]. All non-hydrogen atoms were refined anisotropically, while all hydrogen atoms were located at calculated positions and refined by using riding model. Crystals of 2 displayed twinning and therefore, its structure was refined as a 2-component twin with a transformation matrix of [-1 0 0 / 0 1 0 / 0 0 -1]. Using an HKLF4 refinement in SHELXL, the fractional contribution of the major twin component was refined to 0.54 (4). Details of the data collection and structure refinement are given in Table 2.

Supplementary data

Crystallographic data and refinement parameters of 1 and 2 have been deposited at the Cambridge Crystallographic Data Centre with CCDC numbers 1981760 and 1981761, respectively. These data can be obtained...
Table 2. Crystallographic data and structure refinement for 1 and 2.

|                  | 1                                      | 2                                      |
|------------------|----------------------------------------|----------------------------------------|
| Empirical formula| C_{15}H_{16}ClNO_3PtS                  | C_{22}H_{20}N_2O_6PtS_2                |
| Formula weight   | 520.89                                 | 667.61                                 |
| Crystal system   | monoclinic                             | orthorhombic                           |
| Space group      | P2_1/c                                 | Pnna_2_1                               |
| a, Å             | 8.1776(3)                              | 19.9229(8)                             |
| b, Å             | 12.1960(5)                             | 8.8086(3)                              |
| c, Å             | 16.1270(5)                             | 12.5704(5)                             |
| a, deg           | 90                                     | 90                                     |
| b, deg           | 95.445(3)                              | 90                                     |
| c, deg           | 90                                     | 90                                     |
| V, Å³            | 1601.15(10)                            | 2206.02 (15)                           |
| T, K             | 295(2)                                 | 293(2)                                 |
| Z                | 4                                      | 4                                      |
| \(\rho_{calc}\) (g cm\(^{-3}\)) | 2.161                                  | 2.010                                  |
| \(\mu\) (mm\(^{-1}\)) | 9.071                                  | 6.594                                  |
| \(F(000)\)      | 992                                    | 1296                                   |
| \(\theta\) (°)  | 3.009–25.678                           | 3.003–25.025                           |
| Collected refls | 5261                                   | 7622                                   |
| Data/parameters  | 3011/200                               | 2911/337                               |
| Goodness-of-fit  | 1.012                                  | 1.035                                  |
| \(R_1\) [\(I>2\sigma\)] | 0.0265                                  | 0.0636                                 |
| \(wR_2\)        | 0.0459                                 | 0.1747                                 |
| CCDC number      | 1981760                                | 1981761                                |

free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre.

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References
1. Rosenberg B, Van Camp L, Krigas T. Inhibition of cell division in *Escherichia coli* by electrolysis products from a platinum electrode. Nature 1965; 205: 698-699. doi: 10.1038/205698a0
2. Rosenberg B, Van Camp L, Trosko JE, Mansour VH. Platinum compounds: A new class of potent antitumour agents. Nature 1969; 222: 385-386. doi: 10.1038/222385a0
3. Rosenberg B. Some biological effects of platinum compounds: New agents for the control of tumours. Platinum Metals Review 1971; 15 (2): 42-51.
4. Drew D, Doyle JR. Cyclic diolefin complexes of platinum and palladium. Inorganic Syntheses 1990; 28: 346-349. doi: 10.1002/9780470132593.ch89
5. Otto S, Elding LI. Low temperature kinetic study of very fast substitution reactions at platinum(II) trans to olefins. Journal of the Chemical Society, Dalton Transactions 2002; 11: 2354-2360. doi: 10.1039/b200197g

6. Wandler AEE, Koos MRM, Nieger M, Luy B, Brase S. 1,5-Cyclooctadienyl alcohols and ketones generate a new class of COD Pt complexes. Dalton Transactions 2018; 47 (11): 3689-3692. doi: 10.1039/c8dt00075a

7. Durak LJ, Lewis JC. Transmetalation of alkyl ligands from Cp*(PMe₃)IrR₁R₂ to (cod)PtR₃X. Organometallics 2013; 32 (11): 3153-3156. doi: 10.1021/om400289s

8. Welange NM, Sharp PR. Ethylene oxidation by a platinum(II) hydroxo complex. Insights into the wacker process. Organometallics 2012; 31 (19): 6823-6833. doi: 10.1021/om300626a

9. Jagadeesh MN, Thiel W. Hydroisilylation with bis(alkynyl) (1,5-cyclooctadiene)platinum catalysts: A density functional study of the initial activation. Organometallics 2002; 21 (10): 2076-2087. doi: 10.1021/om0200196

10. McCrindle R, Arsenaульт GJ, Farwaha R, Hampden-Smith MJ, McAlees AJ. A model for the polymerisation of diazomethane by transition metal complexes. Journal of Chemical Society, Chemical Communications 1986; 12: 943-944. doi: 10.1039/C39860000943

11. Cummings SD, Eisenberg R. Luminescent platinum(ii) complexes of quinoxaline-2,3-dithiolate. Inorganic Chemistry 1995; 34 (8): 2007-2014. doi: 10.1021/ic00112a010

12. Hieros J-C, Serp P, Feurer R, Kalck P. MOCVD of rhodium, palladium and platinum complexes on fluidized divided substrates: Novel process for one-step preparation of noble-metal catalysts. Applied Organometallic Chemistry 1998; 12 (3): 161-172. doi: 10.1002/(SICI)1099-0739(199803)12:3<161::AID-AOC689>3.0.CO;2-6

13. Lingen V, Lüning A, Krest A, Deacon GB, Schur J et al. Labile Pd-sulphur and Pt-sulphur bonds in organometallic palladium and platinum complexes [(COD)M(alkyl)(S-ligand)]ⁿ⁺. A speciation study. Journal of Inorganic Biochemistry 2016; 165: 119-127. doi: 10.1016/j.jinorgbio.2016.06.009

14. Lüning A, Neugebauer M, Lingen V, Krest A, Stirnat K et al. Platinum diolefin complexes – Synthesis, structures, and cytotoxicity. European Journal of Inorganic Chemistry 2015; 2: 226-239. doi: 10.1002/ejic.201402954

15. Enders M, Görling B, Braun AB, Seltenreich JE, Reichenbach LF et al. Cytotoxicity and NMR studies of platinum complexes with cyclooctadiene ligands. Organometallics 2014; 33 (15): 4027-4034. doi: 10.1021/om500540x

16. Lüning A, Schur J, Hamel L, Ott I, Klein A. Strong cytotoxicity of organometallic platinum complexes with alkynyl ligands. Organometallics 2013; 32 (13): 3662-3672. doi: 10.1021/om400293u

17. Klein A, Lüning A, Ott I, Hamel L, Neugebauer M et al. Organometallic palladium and platinum complexes with strongly donating alkyl coligands – Synthesis, structures, chemical and cytotoxic properties. Journal of Organometallic Chemistry 2010; 695 (15-16): 1895-1905. doi: 10.1016/j.jorganchem.2010.04.027

18. Butsch K, Elmas S, Sen Gupta N, Gust R, Heinrich F et al. Organoplatinum(II) and -palladium(II) complexes of nucleobases and their derivatives. Organometallics 2009; 28 (13): 3906-3915. doi: 10.1021/om900208r

19. Klein A, Schurr T, Scherer H, Sen Gupta N. Cytosine binding in the novel organoplatinum(II) complex [(COD)PtMe(cytosine)](SbF₆)⁻. Organometallics 2007; 26 (1): 230-233. doi: 10.1021/om060856y

20. Baran EJ, Yılmaz VT. Metal complexes of saccharin. Coordination Chemistry Reviews 2006; 250 (15-16): 1980-1999. doi: 10.1016/j.ccr.2005.11.021

21. Ulukaya E, Arı F, Dimas K, Sarımahmut M, Güney E et al. Cell death-inducing effect of novel palladium(II) and platinum(II) complexes on non-small cell lung cancer cells in vitro. Journal of Cancer Research and Clinical Oncology 2011; 137 (10): 1425-1434. doi: 10.1007/s00432-011-1021-1

22. Güney E, Yılmaz VT, Arı F, Büyükgüngör O, Ulukaya E. Synthesis, characterization, structures and cytotoxic activity of palladium(II) and platinum(II) complexes containing bis(2-pyridylmethyl)amine and saccharinate. Polyhedron 2011; 30 (1): 114-122. doi: 10.1016/j.poly.2010.09.037
23. ArıF, Aktopal N, İçsel C, Yılmaz VT, Güney E et al. Synthesis, structural characterization and cell death-inducing effect of novel palladium(II) and platinum(II) saccharinate complexes with 2-(hydroxymethyl)pyridine and 2-(2-hydroxyethyl)pyridine on cancer cells in vitro. Bioorganic & Medicinal Chemistry 2013; 21 (21): 6427-6434. doi: 10.1016/j.bmc.2013.08.050

24. Cavicchioli M, Massabni AC, Castellano EE, Sabeh LPB, Costa-Neto CM. Synthesis and X-ray structure of the dinuclear platinum(II) complex with saccharin \( \text{K}[\text{Pt(sac)_{3}(H_{2}O)}] \cdot H_{2}O \): Studies on its antiproliferative activity in aqueous solution. Inorganica Chimica Acta 2007; 360 (9): 3055-3060. doi: 10.1016/j.ica.2007.02.040

25. Al-Jibori SA, Al-Jibori GH, Al-Hayaly LJ, Wagner C, Schmidt H et al. Combining anti-cancer drugs with artificial sweeteners: synthesis and anti-cancer activity of saccharinate (sac) and thiosaccharinate (tsac) complexes cis-[Pt(sac)_{2}(NH_{3})_{2}] and cis-[Pt(tsac)_{2}(NH_{3})_{2}]. Journal of Inorganic Biochemistry 2014; 141: 55-57. doi: 10.1016/j.jinorgbio.2014.07.017

26. Yılmaz VT, İçsel C, Turgut ÖR, Aygün M, Erkısa M et al. Synthesis, structures and anticancer potentials of platinum(II) saccharinate complexes of tertiary phosphines with phenyl and cyclohexyl groups targeting mitochondria and DNA. European Journal of Medicinal Chemistry 2018; 155: 609-622. doi: 10.1016/j.ejmech.2018.06.035

27. İçsel C, Yılmaz VT, Aygün M, Cevatemre B, Alper P et al. Palladium(II) and platinum(II) saccharinate complexes with bis(diphenylphosphino)methane/ethane: synthesis, S-phase arrest and ROS-mediated apoptosis in human colon cancer cells. Dalton Transactions 2018; 47 (33): 11397-11410. doi: 10.1039/C8DT02389A

28. Yılmaz VT, İçsel C, Aygün M, Erkısa M, Ulukaya E. Pd(II) and Pt(II) saccharinate complexes of bis(diphenylphosphino)propane/butane: Synthesis, structure, antiproliferative activity and mechanism of action. European Journal of Medicinal Chemistry 2018; 158: 534-547. doi: 10.1016/j.ejmech.2018.09.035

29. İçsel C, Yılmaz VT, Cevatemre B, Aygün M, Ulukaya E. Structures and anticancer activity of chlorido platinum(II) saccharinate complexes with mono- and dialkylphenylphosphines. Journal of Inorganic Biochemistry 2019; 195: 39-50. doi: 10.1016/j.jinorgbio.2019.03.008

30. Syed A, Stevens ED, Cruz SG. Reexamination of the \( \pi \) bonding in dichloro(cycloocta-1,5-diene)platinum. Inorganic Chemistry 1984; 23 (22): 3673-3674. doi: 10.1021/ic00190a053

31. Otto S. Structure and solution behaviour of cyclooctadiene complexes of platinum(II). Inorganica Chimica Acta 2010; 363 (13): 3316-3320. doi: 10.1016/j.ica.2010.06.020

32. Klein A, Klinkhammer K-W, Scheiring T. Cyclooctadienemethylplatinum complexes: synthesis, reactivity, molecular structure and spectroscopic properties of the organometallic hydroxoplatinum(II) complex \([\text{COD}]\text{PtMe(OH)}\). Journal of Organometallic Chemistry 1999; 592 (1): 128-135. doi: 10.1016/S0022-328X(99)00500-8

33. Henderson W, Nicholson BK, McCaffrey LJ. Platinum(II) and palladium(II) saccharinate complexes. Inorganica Chimica Acta 1999; 285 (1): 145-148. doi: 10.1016/S0020-1693(98)00327-2

34. Sheldrick GM. SHELXT–Integrated space-group and crystal structure determination. Acta Crystallographica Section A Foundations and Advances 2015; A71: 3-8. doi: 10.1107/S2053273314026370

35. Sheldrick GM. Crystal structure refinement with SHELXL. Acta Crystallographica Section C Structural Chemistry 2015; C71: 3-8. doi: 10.1107/S2053229614024218

36. Dolomanov OV, Bourhis LJ, Gildea RJ, Howard JAK, Puschmann H. OLEX2: a complete structure solution, refinement and analysis program. Journal of Applied Crystallography 2009; 42 (2): 339-341. doi: 10.1107/S0021889808042726