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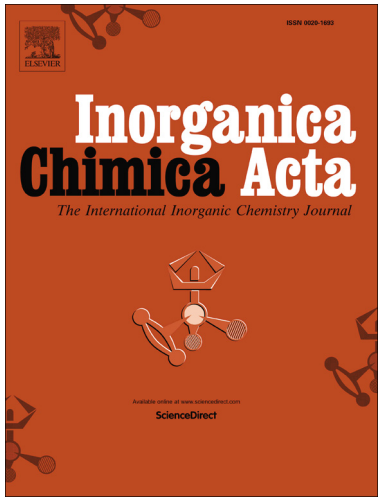

Research paper

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Synthesis and reactivity of platinum(II) triphenylphosphino complexes with aromatic aldoximes

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Dedicated to Dr Carlo Mealli on occasion of his 70th birthday

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Abstract: *trans*-[Pt(μ-Cl)Cl(PPh_3)]$_2$ reacted with arylaldoximes in 1,2-dichloroethane to afford [$PtCl_2(PPh_3)${N(OH)=CHAr}] (Ar = 3,4-dimethoxyphenyl, 1-naphthyl, 9-anthryl) where aldoxime ligands are N-coordinated to platinum. The obtained complexes are soluble in chlorinated solvents, where they afford equilibrium mixtures of *cis,trans* and/or *(E),(Z)* isomers. Equilibria in solution were studied by ^{31}P-NMR spectroscopy and solid state structural data were obtained by single crystal X ray diffraction studies. The reactivity of [$PtCl_2(PPh_3)${N(OH)=CHAr}] complexes with basic aqueous solutions was studied, under liquid-liquid phase transfer catalysis conditions. The outcome of the reaction depends on the stereochemistry of the precursors: *cis,*(Z)-isomers promptly undergo cyclization to the corresponding dinuclear derivatives [Pt{μ-(κ^2-N,O)}-{N(O)=CHAr}Cl(PPh_3)]$_2$, where two aldoximate ligands symmetrically bridge two metal centers.

Keywords: platinum(II); triphenylphosphine; *cis-trans* isomerism; cyclization; phase transfer catalysis.

1. Introduction

Since the early discover of anticancer properties of *cis*-[$PtCl_2(NH_3)_2$][1], many studies have been carried out with the aim of elucidating the mechanism of action of platinum based drugs [2] and it is generally accepted that the main target of these bioactive molecules is DNA. The platination of DNA generally involves the coordination of purine bases to activated, hydrolyzed forms of the metal complexes and can be greatly helped by additional interactions such as hydrogen bonding. As a matter of fact, good results have been described for some platinum complexes characterized by the presence of OH groups on coordinated ligands [3]. In the context of our studies on platinum(II) derivatives [4], we have observed interesting antiproliferative properties for triphenylphosphino

complexes [4a-f]. In particular, *trans*-[$PtCl_2(PPh_3)$(DEA)] (DEA = diethanolamine) [4d,f], where the ligated amine bears two hydroxyl groups, was found more active than cisplatin towards HeLa cells. Moreover, it is worth to note that hydroxyl functional groups are reactive towards a series of chemical transformations, so that platinum compounds bearing OH groups could be good precursors to more complex derivatives. We report here the synthesis, characterization and reactivity under basic conditions of three complexes [$PtCl_2(PPh_3)${N(OH)=CHAr}] (Ar = 3,4-dimethoxyphenyl, 1-naphthyl, 9-anthryl), bearing, besides PPh_3, a coordinated arylaldoxime.

2. Experimental

2.1. Materials and general methods

All manipulations were performed under a dinitrogen atmosphere, if not otherwise stated. Solvents and liquid reagents were dried according to reported procedures [5]. ^{1}H-, ^{13}C-, ^{31}P- and ^{195}Pt-NMR spectra were recorded with a Bruker ''Avance DRX400'' spectrometer, in $CDCl_3$ solution if not otherwise stated. Chemical shifts were measured in ppm (δ) from TMS by residual solvent peaks for ^{1}H and ^{13}C, from aqueous (D_2O) H_3PO_4 (85%) for ^{31}P and from aqueous (D_2O) hexachloroplatinic acid for ^{195}Pt. A sealed capillary containing C_6D_6 was introduced in the NMR tube to lock the spectrometer to the deuterium signal when non-deuterated solvents were used. FTIR spectra in solid phase were recorded with a Perkin–Elmer ''Spectrum One'' spectrometer, equipped with an ATR accessory. Elemental analyses (C, H, N) were performed at Dipartimento di Scienze e Tecnologie Chimiche, Università di Udine. *Trans*-[$Pt(\mu\text{-}Cl)Cl(PPh_3)]_2$ [4h] was prepared according to a reported procedure. Aldoxime ligands ArCH=N(OH) [Ar = 3,4-dimethoxyphenyl (**1**), 1-Naphtyl (**2**), 9-Anthryl (**3**)] were prepared by a slight modification of a described procedure.[6] In the text the following abbreviations were used: 1,2-dichloroethane (1,2-DCE), tetrabutylammonium chloride (TBACl).

2.2.Synthesis of platinum complexes [$PtCl_2(PPh_3)${N(OH)=CHAr}]

*2.2.1. [$PtCl_2(PPh_3)${N(OH)=CH($C_6H_3(OMe)_2$)}] ([$PtCl_2(PPh_3)$(**1**)], **4**)*

A sample (0.300 g) of *trans*-[$Pt(\mu\text{-}Cl)Cl(PPh_3)]_2$ [4h] (0.56 mmol of Pt) was suspended in 1,2-DCE (15.0 mL) and treated with a solution of aldoxime **1** (0.101 g) in the same solvent (**1**/Pt molar ratio= 1.0). The suspension was stirred at room temperature (1h) and then treated with another portion (0.101 g) of ligand **1** and refluxed (84 °C). The initially orange suspension turned into a yellow solution and a colorless solid formed. The solid was filtered and dried under vacuum (0.100 g). A sample of this solid was crystallized from a $CHCl_3$ solution, by slow diffusion of pentane vapors and identified (single crystal X-ray diffraction) as (Z)-*cis*-[$PtCl_2(PPh_3)$(**1**)] {(Z)-*cis*-**4**}. The ^{31}P-

NMR spectrum of a freshly prepared $CDCl_3$ solution of the crystals showed a signal at 5.60 ppm ($^1J_{P\text{-}Pt}$ = 3860 Hz). The ^{31}P-NMR spectrum of another sample of the crystals dissolved in 1,2-DCE showed after 2h four signals: 5.29 (69%), 2.46 (27%), 1.33 (4%), 7.37 (traces). The isomer responsible of the ^{31}P-NMR signal at 2.46 ppm was crystallized and identified (single crystal X-ray diffraction) as (E)-*trans*-[$PtCl_2(PPh_3)$(**1**)] {(E)-*trans*-**4**}. A second crop of product was precipitated as a mixture of isomers (total isolated yield 51%). We report the spectroscopic characterization for the species (Z)-*cis*-**4** and (E)-*trans*-**4**.

(Z)-*cis*-**4**. $C_{27}H_{28}Cl_2NO_4PPt$ Anal. Calc.: C 44.6, H 3.9, N 1.9 %; Exp.: C 44.8, H 4.4, N 2.0. FTIR (ATR, cm^{-1}): 3159 ($\tilde{\upsilon}$ OH), 3048 ($\tilde{\upsilon}$ CH), 2992 ($\tilde{\upsilon}$ CH), 1623 ($\tilde{\upsilon}$ CN). ^{1}H-NMR: 8.66 (d, 1H, $^4J_{H\text{-}P}$=4 Hz, C<u>H</u>N); 8.32 (bs, 1H, O<u>H</u>); 7.78 (s, 1H, H_{arom}); 6.86 (d, 1H, J=8.9 Hz, H_{arom}); 7.53-7.45 (m, 10H, H_{arom} + H_{arom} PPh_3); 7.36-7.32 (m, 6H, H_{arom} PPh_3) 4.05 (s, 3H, OC<u>H</u>$_3$); 3.98 (s, 3H, OC<u>H</u>'$_3$). ^{31}P-NMR: 5.60 ($^1J_{P\text{-}Pt}$=3860 Hz).

(E)-*trans*-**4**. ^{1}H-NMR: 10.9 (s, 1H, O<u>H</u>); 8.45 (d, $^4J_{H\text{-}P}$=3 Hz, C<u>H</u>N); 7.82-7.78 (m, 6H, H_{arom} PPh_3); 7.73 (s, 1H, H_{arom}); 7.59 (d, 1H, J= 8.6 Hz, H_{arom}); 7.58-7.46 (m, 9H, H_{arom} PPh_3); 6.94 (d, J=8.6 Hz, H_{arom}); 3.97 (s, 3H, OC<u>H</u>$_3$); 3.92 (s, 3H, OC<u>H</u>'$_3$). ^{31}P-NMR: 2.54 ($^1J_{P\text{-}Pt}$=3658 Hz).

*2.2.2. [$PtCl_2(PPh_3)${N(OH)=CH(1-Naphtyl)}] ([$PtCl_2(PPh_3)$(**2**)], **5**)*

A sample (0.194 g) of *trans*-[Pt(μ-Cl)Cl(PPh_3)]$_2$ [4h] (0.36 mmol of Pt) was suspended in 1,2-DCE (15.0 mL) and treated with a solution of aldoxime **2** (0.064 g) in the same solvent (**2**/Pt molar ratio= 1.0). The suspension was refluxed (84 °C) 24h. The initially orange suspension turned into a yellow solution and a colorless solid formed. The solid was filtered and dried under vacuum (0.061 g) and identified as (Z)-*cis*-**5**. The liquid phase was refluxed (12h) and treated with heptane. A second crop of solid was obtained and identified as (E)-*trans*-**5**. The total, isolated yield was 60%. We report the spectroscopic characterization for the species (E)-*trans*- and (Z)-*cis*-**5**.

(Z)-*cis*-**5**. $C_{29}H_{24}Cl_2NOPPt$. Anal. Calc.: C 49.8, H 3.5, N 2.0 %; Exp.: C 49.4, H 4.0, N 2.0%. FTIR (ATR, cm^{-1}): 3117 ($\tilde{\upsilon}$ OH), 3049 ($\tilde{\upsilon}$ CH), 3006 ($\tilde{\upsilon}$ CH), 1618 ($\tilde{\upsilon}$ CN). ^{1}H-NMR: 9.85 (d, 1H, J=7 Hz, H_{arom}); 8.81 (s, 1H, O<u>H</u>); 8.78 (d, 1H, C<u>H</u>N); 8.08 (d, 1H, J=8.4 Hz, H_{arom}); 7.88 (d, 1H, J=8.3 Hz, H_{arom}); 7.78 (dd, 1H, J=J'= 7.7 Hz, H_{arom}); 7.52 (dd, 1H, J=J'= 7.3 Hz, H_{arom}); 7.38-7.30 (m, 10H, H_{arom} + H_{arom} PPh_3); 7.21-7.18 (m, 6H, H_{arom} PPh_3), 6.89 (d, 1H, J=8.2Hz, H_{arom}). ^{31}P-NMR: 5.60 ($^1J_{P\text{-}Pt}$=3860 Hz).

(E)-*trans*-**5**. ^{1}H-NMR: 11.05 (d, 1H, J=3.4 Hz, O<u>H</u>); 9.46 (d, 1H, J= 2.5 Hz, C<u>H</u>N); 8.40 (d, 1H, J=7.3 Hz, H_{arom}); 8.14 (d, 1H, J=8.1 Hz, H_{arom}); 8.00 (d, 1H, J=8.1 Hz, H_{arom}); 7.90 (d, 1H, J=7.3 Hz, H_{arom}); 7.86-7.82 (m, 6Hz, H_{arom} PPh_3); 7.60-7.45 (m, 12H, H_{arom}+ H_{arom} PPh_3). ^{13}C-NMR: 148.7, 134.8 (d, $J_{C\text{-}P}$= 10.5 Hz),

133.5, 132.1, 131.7, 131.3, 131.2, 129.7, 128.8, 128.5 (d, J_{C-P}= 64 Hz), 128.1 (d, J_{C-P}= 11.7 Hz), 127.5, 126.4, 125.0, 123.6. ^{31}P-NMR: 2.38 ($^{1}J_{P-Pt}$=3678 Hz). ^{195}Pt-NMR: -3610 ($^{1}J_{P-Pt}$=3678 Hz).

*2.2.3. [$PtCl_2(PPh_3)${N(OH)=CH(9-Anthryl)}] ([$PtCl_2(PPh_3)$(**3**)], **6**)*

A sample (0.301 g) of *trans*-[Pt(μ-Cl)Cl(PPh_3)]$_2$ [4h] (0.59 mmol of Pt) was suspended in 1,2-DCE (15.0 mL) and treated with a solution of aldoxime **3** (0.129 g) in the same solvent ([**3**]/[Pt] molar ratio = 1.0). The suspension, stirred at room temperature for 4h, at first turned into a yellow solution and successively a yellow solid formed. The solid was filtered and dried under vacuum (0.167 g). A sample of the solid, dissolved in $CDCl_3$, was studied spectroscopically (^{31}P-NMR, ppm): 1.58 ($^{1}J_{P-Pt}$ = 3781 Hz). After 48 h the spectrum showed the signal at 1.58 (20%, $^{1}J_{P-Pt}$ = 3781 Hz) and a new one at 2.29 (80%, $^{1}J_{P-Pt}$ = 3705 Hz). From this mixture the species responsible of the signal at 2.29 ppm was crystallized and identified (single crystal X-ray diffraction) as (E)-*trans*-**6.** A second crop of solid was collected (0.065 g) for a total yield of 54%. We report the spectroscopic characterization for the species (Z)-*trans*-**6** and (E)-*trans*-**6**.

(Z)-*trans*-**6**. $C_{33}H_{26}Cl_2NOPPt$. Anal. Calc.: C 52.9, H 3.5, N 1.9 %; Exp.: C 52.7, H 4.1, N 1.9%. FTIR (ATR, cm^{-1}): 3188 ($\tilde{\nu}$ OH), 3058 ($\tilde{\nu}$ CH), 1627 ($\tilde{\nu}$ CN). ^{1}H-NMR: 9.61 (d, 1H, $^{4}J_{H-P}$=9.0 Hz, $^{3}J_{H-Pt}$=50 Hz, C<u>H</u>N); 9.45 (s, 1H, O<u>H</u>); 8.66 (s, 1H, H_{arom}); 8.44 (d, 2H, J=8.7 Hz, H_{arom}); 8.11 (d, 2H, J=8.4 Hz, H_{arom}); 7.66 (m, 2H, H_{arom}); 7.56 (m, 2H, H_{arom}); 7.39-7.23 (m, 15H, H_{arom} PPh_3). ^{13}C-NMR: 155.4, 134.5 (d, J_{C-P}= 10.4 Hz), 131.2, 130.8, 130.5, 130.4, 128.7, 127.7 (d, J_{C-P}= 11.5 Hz), 127.6 (d, J_{C-P}= 66.7 Hz), 127.0, 125.7, 125.6, 123.3. ^{31}P-NMR: 1.58 ($^{1}J_{P-Pt}$=3781 Hz). ^{195}Pt-NMR: -3559 ($^{1}J_{P-Pt}$=3781 Hz).

(E)-*trans*-**6**. ^{1}H-NMR: 10.87 (s, 1H, O<u>H</u>); 9.69 (d, 1H, $^{4}J_{H-P}$=2.0 Hz, $^{3}J_{H-Pt}$=20 Hz, C<u>H</u>N); 8.59 (s, 1H, H_{arom}); 8.06 (d, 2H, J=8.4 Hz, H_{arom}); 8.03 (d, 2H, J=8.7 Hz, H_{arom}); 7.90-7.85 (m, 6H, H_{arom} PPh_3); 7.61-7.56 (m, 4H, H_{arom}); 7.56-7.49 (m, 9H, H_{arom} PPh_3). ^{13}C-NMR:152.2, 134.9 (d, J_{C-P}= 10.3 Hz), 131.3, 131.0, 130.0, 128.9, 128.4, 128.1 (d, J_{C-P}= 11.4 Hz), 128.0 (d, J_{C-P}= 69.0 Hz), 127.0, 125.7, 125.3 (2C); ^{31}P-NMR: 2.29 ($^{1}J_{P-Pt}$=3691 Hz). ^{195}Pt-NMR: -3614 ($^{1}J_{P-Pt}$=3691 Hz).

2.3.General procedure for the base promoted cyclodimerization reaction

A 1,2-DCE solution of [$PtCl_2(PPh_3)${N(OH)=CHAr}] (0.2 mmol in 15 mL) was mixed with an aqueous solution of NaOH (0.4 mmol in 15mL). A catalytic amount (about 10 mg) of TBACl was added and the mixture was refluxed under vigorous stirring (2h). The disappearance of the precursor was checked by ^{31}P-NMR spectroscopy, together with the appearance of a single new signal at -0.858 ($^{1}J_{P-Pt}$= 3981 Hz) and the two phases were separated. The aqueous phase was extracted with portions of $CHCl_3$ (3 x 5 mL) and all the collected organic phases were dried over anhydrous Na_2SO_4. The solution was concentrated under vacuum and then treated with heptane

under stirring. A pale yellow solid formed which was filtered and dried under vacuum. For each compound, the precursor used, the isolated product yield and the spectroscopic characterization is reported:

*2.3.1. (SP4,4; SP4,4)-(Z, Z)-[PtCl{μ-(κ²-N,O)-(**1**–H)}(PPh₃)]₂ [(SP4,4; SP4,4)-(Z, Z)-**7**].* (Z)-*cis*-**4** (50% yield). FTIR (ATR, cm^{-1}): 3059 ($\tilde{\upsilon}$ CH), 1598 ($\tilde{\upsilon}$ CN). ^{1}H-NMR: 8.11 (d, 1H, C<u>H</u>N); 7.73 (m, 7H, H_{arom} + H_{arom} PPh_3); 7.39-7.25 (m, 9H, H_{arom} PPh_3); 7.01 (s, 1H, H_{arom}); 6.82 (d, 1H, H_{arom}); 3.92 (s, 3H, OC<u>H</u>$_3$); 3.83 (s, 3H, OC<u>H'</u>$_3$). ^{13}C-NMR: 150.7; 148.3; 134.8; 134.6 (d, J_{C-P}=10 Hz); 130.6; 128.4 (d, J_{C-P}=64 Hz); 127.8 (d, J_{C-P}=11 Hz); 124.3; 121.6; 111.3; 110.4; 56.1; 55.0. ^{31}P-NMR: -0.801 ($^{1}J_{P-Pt}$= 3974 Hz). ^{195}Pt-NMR: -3251 ($^{1}J_{P-Pt}$= 3974 Hz).

*2.3.2. (SP4,4; SP4,4)-(Z, Z)-[PtCl{ μ-(κ²-N,O)-(**2**–H)}(PPh₃)]₂ [(SP4,4; SP4,4)-(Z, Z)-**8**].* (Z)-*cis*-**5** (48 % yield). FTIR (ATR, cm^{-1}): 3057 ($\tilde{\upsilon}$ CH), 1571 ($\tilde{\upsilon}$ CN). ^{1}H-NMR: 9.42 (d, 1H, H_{arom}); 8.72 (s, 1H, C<u>H</u>N); 7.92 (d, 1H, H_{arom}); 7.76 (d, 1H, H_{arom}); 7.65 (m, 1H, H_{arom}); 7.55-7.44 (m, 4H, H_{arom} + H_{arom} PPh_3); 7.41-7.32 (m, 7H, H_{arom} + H_{arom} PPh_3);7.23-7.10 (m, 6H, H_{arom} PPh_3); 6.68 (d, 1H, H_{arom}). ^{13}C-NMR: 150.1; 147.6; 140.0; 134.4 (d, J_{C-P}=10 Hz); 133.0; 130.5; 128.5 (d, J_{C-P}=68 Hz); 128.4; 128.2; 127.8; 126.5; 126.0 (2C); 125.4; 123.5. ^{31}P-NMR: -1.58 ($^{1}J_{P-Pt}$= 3986 Hz). ^{195}Pt-NMR: -3229 ($^{1}J_{P-Pt}$= 3986 Hz).

2.4. X-ray structure determination

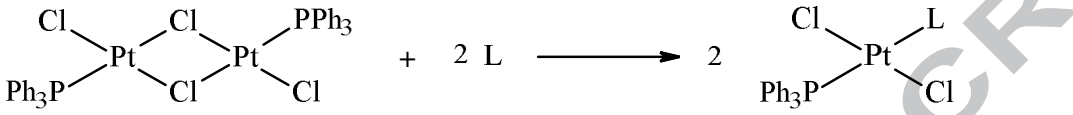
Crystals were selected at room temperature (296 K), glued to glass fibers and analyzed with a Bruker Smart Breeze CCD diffractometer. Table 1 summarizes the lattice parameters and the respective space groups. Intensity data were collected in the ranges of 2θ angles reported in the Table. After correction for Lorentz and polarization effects and for absorption, the structure solutions were obtained using the direct methods contained in SHELXS program.[7] The asymmetric units of all the three crystals correspond to the respective molecules but in the case of (Z)-*cis*-**4** and (E)-*trans*-**6** ones the structures are completed by a solvent molecule: chloroform and *n*-pentane, respectively. The *n*-pentane solvent molecules are disordered and had to be introduced in the model by fitting a molecule with an idealized geometry over the residual maxima of the difference Fourier map and refined as a rigid group. All the hydrogen atoms were introduced in calculated positions. The final reliability factors and some details of the refinement procedure are listed in Table S3.

The structure refinement was done using SHELXL program,[8] other control calculations were performed with the programs contained in the suite WINGX.[9]

3. Results and discussion

3.1 Synthesis of arylaldoxime Pt complexes.

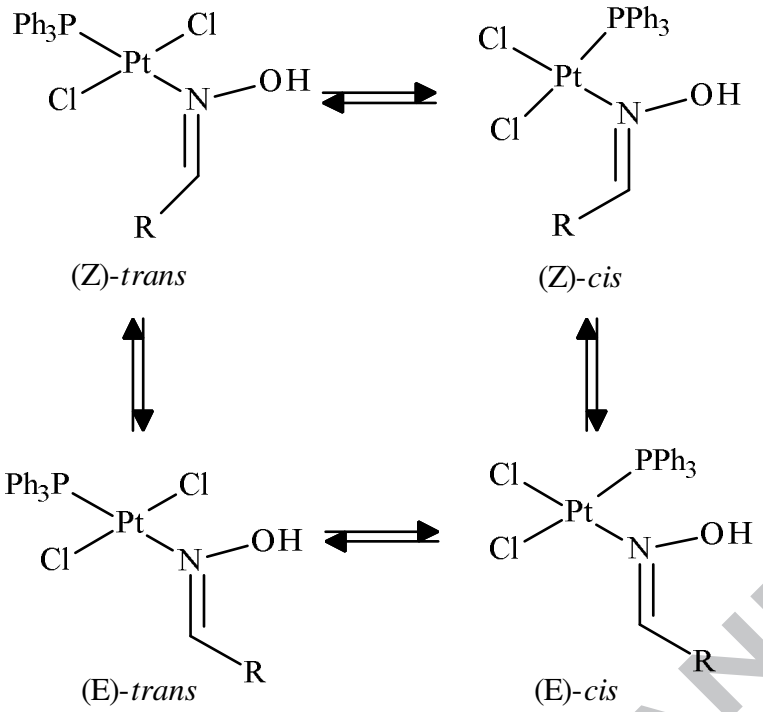
Arylaldoxime ligands were prepared in good yields by a slight modification of a described procedure [6] and were used to synthesize the corresponding platinum(II) complexes according to the regio- and stereoselective ring-opening reaction of *trans*-[Pt(μ-Cl)Cl(PPh_3)]$_2$[4h] depicted in Scheme 1.



L = Arylaldoxime

Scheme 1. Ring-opening reaction leading to complexes [$PtCl_2(PPh_3)${N(OH)=CHAr}]

Although oxime ligands show both N- or O-coordination to metals [10], in the case of platinum(II) N-coordination is much more frequently observed [3b,10,11], with the exception of cases where deprotonated oximes act as anionic ligands [3a]. In our case, taking into account the strong trans effect exerted by PPh_3, the reaction of arylaldoximes with *trans*-[Pt(μ-Cl)Cl(PPh_3)]$_2$ (Scheme 1) was expected to afford *trans* platinum complexes with N-coordinated oxime ligands. Nevertheless, since square planar Pt(II) complexes often show *cis/trans* isomerization equilibria in solution and arylaldoxime ligands can show (E)/(Z) isomerism as well, up to four complexes could theoretically be observed (Scheme 2). With the aim of following the reaction and characterize spectroscopically the species formed, a sample (30.0 mg) of *trans*-[Pt(μ-Cl)Cl(PPh_3)]$_2$ was reacted with a slight excess of arylaldoxime **1** in $CDCl_3$. ^{31}P-NMR analysis clearly showed the formation, after only few minutes, of a kinetic product (1.25 ppm, $^1J_{P\text{-}Pt}$=3693 Hz), which was reasonably ascribed to (Z)-*trans*-[$PtCl_2(PPh_3)${N(OH)=CH($C_6H_3(OMe)_2$)}] (Scheme 2, (Z)-*trans*-**4**). Indeed, the chemical shift and the $^1J_{P\text{-}Pt}$ coupling constant measured in (Z)-*trans*-**4** were very similar to those measured in Pt(II) complexes were a PPh_3 group is *trans* to ligands coordinated *via* an sp^2 nitrogen atom [4a]. On the other hand, (Z) geometry in the complex was assigned taking into account the most likely (E) geometry for the free ligand in solution. The complex was characterized in solution also by ^{1}H-, ^{13}C- and ^{195}Pt-NMR (see SI-2).



Scheme 2. Possible equilibria involving $[PtCl_2(PPh_3)\{N(OH)=CHAr\}]$ complexes.

Besides the signal corresponding to the kinetic product (Z)-*trans*-**4**, two other minor signals with satellites (2.54 ppm, $^1J_{P\text{-}Pt}$=3668 Hz, 6% and 5.60 ppm, $^1J_{P\text{-}Pt}$=3890 Hz, traces) were soon observed in the ^{31}P-NMR spectrum, clearly indicating the presence of equilibria in solution. The relative intensities of the signals changed with time (Table S1) and, after 24h, some colorless crystals formed, which were identified as (Z)-*cis*-**4** by single crystal X-ray diffraction. ^{31}P-NMR analysis carried out on a freshly prepared solution of (Z)-*cis*-**4** in $CDCl_3$ allowed to assign to this complex the resonance at 5.60 ppm ($^1J_{P\text{-}Pt}$=3890 Hz). When a sample of (Z)-*cis*-**4** was dissolved in refluxing 1,2-DCE, a yellow solution was obtained. ^{31}P-NMR spectrum registered on the same solution at room temperature showed four signals (5.29 {69%, $^1J_{P\text{-}Pt}$=3857 Hz}, 2.46 {27%, $^1J_{P\text{-}Pt}$=3664 Hz}, 1.33 {4%, $^1J_{P\text{-}Pt}$=3700 Hz}, 7.33 {traces}). While signals at 5.29 and 1.33 belonged to the aforementioned (Z)-*cis*-**4** and (Z)-*trans*-**4**, the product characterized by the signal at 2.46 ppm was crystallized and identified as (E)-*trans*-**4** by single crystal X-ray diffraction, so that it was possible to assign the resonance at 7.33 ppm to (E)-*cis*-**4**. When the synthesis of complex **4** was carried out in 1,2-DCE on a preparative scale, (Z)-*cis*-**4** precipitated out of the reaction mixture and was recovered pure, while a second crop of solid was obtained as a mixture of isomers and the overall yield was about 50%. Analogous preparations were carried out using arylaldoximes **2** and **3** and the complexes were identified on the basis of their ^{31}P-NMR chemical shifts and coupling constants. In all cases studied the formation of a kinetic product was observed, followed by its isomerization.

With naphthalene derivative **2** it was possible to obtain the least soluble (Z)-*cis*-**5** isomer in good yield, while with the anthracene derivative **3**, isomerization to *cis* isomers was not observed, probably due to steric hindrance: in this case, the kinetic product (Z)-*trans*-**6** precipitated out (54%) from the reaction mixture and was characterized spectroscopically. A sample of (Z)-*trans*-**6** slowly isomerized in $CHCl_3$ solution to (E)-*trans*-**6**, which was crystallized by addition of pentane. Its structure was determined by single crystal X-ray diffraction. A schematic representation of the identified isomers for complexes **4**-**6**, with the corresponding ^{31}P-NMR observed signals, is depicted in Chart 1.

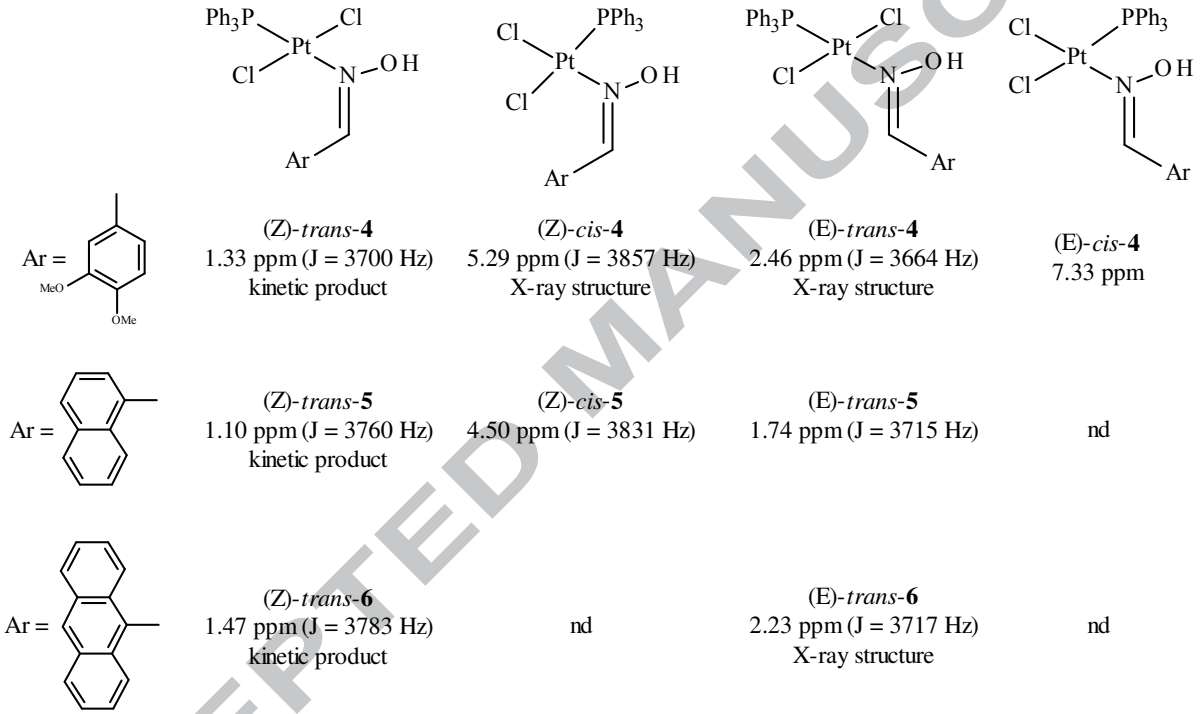


Chart 1. ^{31}P-NMR data in 1,2-DCE solution for complexes **4**-**6**.

With a similar procedure *trans*-[Pt(μ-Cl)Cl(PPh_3)]$_2$ was reacted with 1,3-diphenylpropan-2-one oxime (**S1**). In this case only *cis/trans* isomerism was possible, since the oxime was obtained from a symmetric ketone. The kinetic *trans* isomer (**S2**) was characterized in solution (Table S1), while the less soluble *cis*-**S2** was recovered in good yield (SI-4).

All the prepared oxime Pt(II) complexes were not soluble in water nor ethanol. They were soluble, but not stable in DMSO. As a matter of fact, ^{31}P-NMR spectra registered in DMSO solutions of compounds **4**-**6** showed their conversion into *cis*-[$PtCl_2(PPh_3)$(DMSO)] (18.15 ppm, $^1J_{P\text{-}Pt}$ = 3772 Hz) [4d]. C*is* isomers reacted slower than *trans* isomers, anyway in all cases the substitution reaction was complete within 48h. This behavior is due to the strong *trans* effect exerted by PPh_3.

3.2 Reactivity of arylaldoxime Pt complexes with NaOH under phase transfer catalysis conditions.

It is known [10,12] that the acidity of oxime hydroxyl group is enhanced upon coordination to metal centers. This reactivity has been used [3a] to prepare dinuclear derivatives upon treatment of some bis(oxime)dichloroplatinum complexes with silver acetate. It seemed then interesting to investigate the behavior of arylaldoxime complexes towards bases. In a preliminary experiment, a solution of (E)-*trans*-**6** in 1,2-DCE was treated with an aqueous solution of NaOH, in the presence of a catalytic amount of tetrabutylammonium chloride. The mixture was refluxed and the reaction was monitored by ^{31}P-NMR spectroscopy. The analysis of the spectrum showed the presence of several signals, which were not assigned. An analogous behavior was observed when (E)-*trans*-**5** was used. The outcome of the reaction did not change when the process was carried out at room temperature. On the contrary, good results were obtained when (Z)-*cis*-**4** was reacted under the same experimental conditions. After two hours, the ^{31}P-NMR signal due to (Z)-*cis*-**4** had disappeared and a single, new signal with satellites was observed (-0.807 ppm, $^{1}J_{P\text{-}Pt}$=3974 Hz). A yellow solid was recovered upon the usual work-up and addition of pentane. The ^{1}H-NMR analysis in $CDCl_3$ showed the absence of the OH signal of the precursor, while other signals were significantly shifted. The complete conversion of the precursor was evident also in the ATR-FTIR spectrum of the recovered solid, where the strong absorption at 3159 cm^{-1}, due to OH stretching, had disappeared. The slow diffusion of pentane vapours into a $CHCl_3$ solution afforded crystals, which allowed the structural determination (Figure S1) of the dinuclear derivative (SP4,4; SP4,4)-(Z, Z)-[PtCl{μ-(**1**–H)}(PPh_3)]$_2$ (Figure 1), where two monoanionic aldoximate ligands coordinate two platinum centers in a head-to-tail mode. To the best of our knowledge, only another example of this kind is described.[3a] In a similar way, a single product was obtained starting from (Z)-*cis*-**5.** Despite several attempts, it was not possible to crystallize the complex, but its ATR-FTIR and NMR spectroscopic features, very similar to those observed in the case of [(SP4,4; SP4,4)-(Z, Z)-**7**], allowed to identify it as (SP4,4; SP4,4)-(Z, Z)-[PtCl{μ-(**2**–H)}(PPh_3)]$_2$ [(SP4,4; SP4,4)-(Z, Z)-**8**] (Figure 1).

These data show that the selectivity observed in the formation of dinuclear complexes **7** and **8** depends on the stereochemistry of the precursor, the *cis* isomers allowing the formation of the dinuclear complex more quickly than possible other products. This data is in agreement with the behavior previously observed in DMSO.

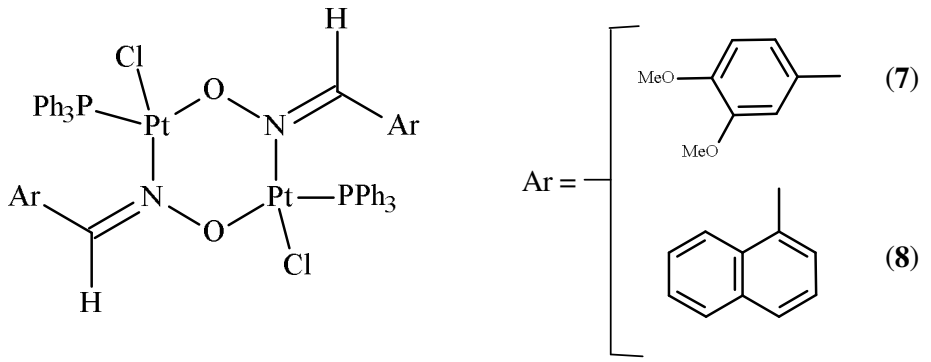


Figure 1. Structure of dinuclear complexes **7** and **8**.

3.3 Structural determinations

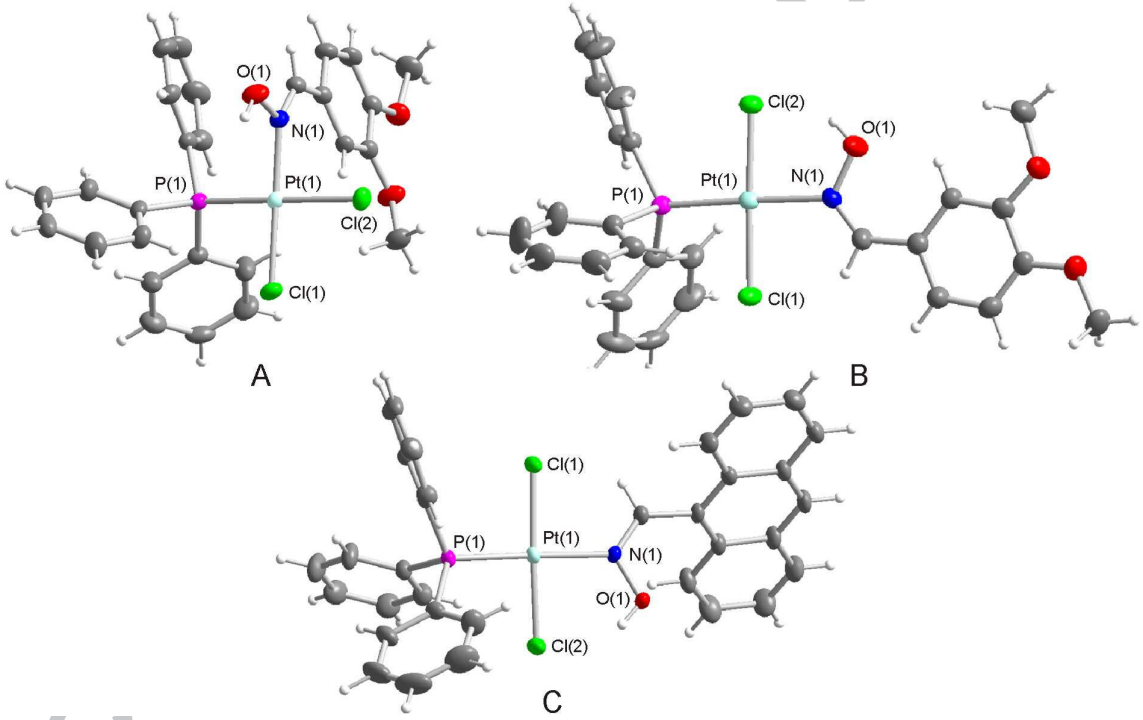


Figure 2. Structures of (Z)-*cis*-**4** (A), (E)-*trans*-**4** (B) and (E)-*trans*-**6** (C).

The structures of complexes (Z)-*cis*-**4**, (E)-*trans*-**4** and (E)-*trans*-**6** are reported in Figure 2 (A, B and C respectively), while the most significant bond lengths and angles for the three derivatives are listed in Table S2. In all the complexes, the coordination around platinum is square planar, with small deviations from ideality. Oxime ligands are N-coordinated to the metal, as in most of the described oxime platinum(II) complexes. In (Z)-*cis*-**4** the Pt–N bond length (2.014(3) Å) is in good agreement with data described for [PtX_2(N-oxime)(L)] complexes (X = halide, L = N-coordinated

oxime, DMSO) [13], where Pt–N bond lengths range from 1.90(2) Å to 2.051(9) Å. The molecules of (Z)-cis-**4** are held in couples by OH···Cl interactions with O(1)···Cl(2') distance of 3.08 Å as shown in Figure S2.

In (E)-*trans*-**4** and (E)-*trans*-**6** the Pt–N bond lengths are significantly longer (2.134(3) and 2.1393(16) respectively), due to the *trans* influence exerted by triphenylphosphine and already observed for some dipyridyl- and piperazino- Pt(II) complexes. [4a] Indeed, these bond lengths can be compared with those reported for *trans*-hydrido(3-methylisoxazol-4,5-dion-4-oximato-N)bis(triphenylphosphino)platinum(II) [14] (2.15(3) Å) and for some platinum acetyl(N-oxime) derivatives [15] (bond lengths ranging from 2.104(3) to 2.137(3) Å), where the N-coordinated oxime ligand is *trans* to residues (hydride and acetyl) characterized as well by a strong *trans* influence. Couples of molecules of (E)-trans-**6** interacts by π-stacking of phenanthryl moieties at distance of about 3.5 Å, as shown in Figure S3.

4. Conclusions

New dichloroplatinum(II) complexes bearing PPh_3 and arylaldoxime ligands were prepared starting from *trans*-$[PtCl(\mu\text{-}Cl)(PPh_3)]_2$ and arylaldoximes. In each case, coordination to platinum involved nitrogen and the kinetic (Z)-*trans*- product formed at first. Anyway, equilibria in solution involving *cis/trans* and/or (E)/(Z) stereoisomers were observed. The study of these equilibria by NMR spectroscopy, together with X-ray diffraction on solid samples, allowed to describe completely the investigated systems. While (E)/(Z) isomerism involving the oxime C=N double bond was observed in all cases studied, *cis/trans* equilibria were affected by steric hindrance; as a matter of fact, with anthryl-9-carbaldoxime **3**, only *trans* isomers were obtained. It is worth to note that *cis* isomers were generally less soluble than the corresponding *trans* derivatives and could be obtained as pure samples.

$[PtCl_2(PPh_3)\{N(OH)=CH(Ar)\}]$ complexes reacted promptly with aqueous NaOH, under PTC conditions and the outcome of the reaction was affected by stereochemistry. While *trans* isomers afforded mixtures of unidentified products, (Z)-*cis*-**4** and (Z)-*cis*-**5** were converted cleanly into rare dinuclear aldoximate complexes (SP4,4; SP4,4)-(Z,Z)-$[PtCl\{\mu\text{-}(\mathbf{1}\text{–}H)\}(PPh_3)]_2$ (**7**) and (SP4,4; SP4,4)-(Z, Z)-$[PtCl\{\mu\text{-}(\mathbf{2}\text{–}H)\}(PPh_3)]_2$ (**8**). Since the process is stereospecific, the steric hindrance of *cis* mononuclear precursors is maintained in the dinuclear products **7** and **8**. Thus, the loss of selectivity observed with *trans* isomers has to be sought in their higher reactivity, due to the strong *trans* effect exerted by PPh_3. The different reactivity of the two isomers is in agreement with the

behavior previously observed in DMSO. Although for both isomers thecoordinated oxime is substituted by DMSO, *trans*-**4**-**6** reacted faster than the corresponding *cis* isomers. The prompt and clean reactivity observed for the aforementioned (Z)-*cis*- complexes **4** and **5** under basic PTC conditions is promising, in view of their further derivatization.

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Appendix A. Supplementary data

Experimental details concerning the preparation of **5** as well as some spectroscopic data are reported as Supplementary Information.

CCDC 1535199-1535202 contain the supplementary crystallographic data for the derivatives (Z)-*cis*-**4** , (E)-*trans*-**4** , (E)-*trans*-**6** and [(SP4,4; SP4,4)-(Z, Z)-**7**]. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif

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Synthesis and reactivity of platinum(II) triphenylphosphino complexes with aromatic aldoximes

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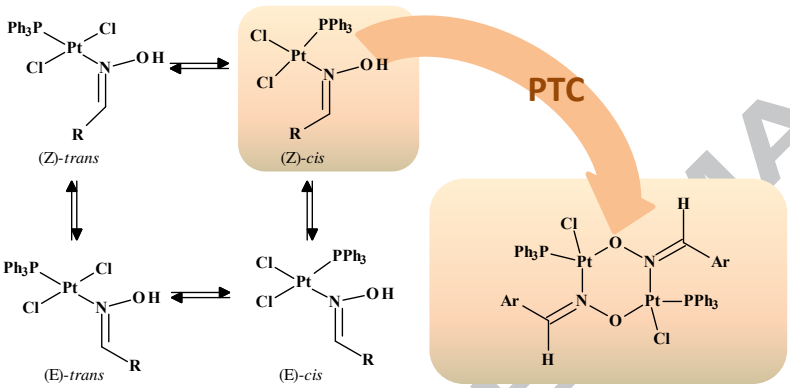
Graphical Abstract



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Highlights

- *trans*-[Pt(μ-Cl)Cl(PPh_3)]$_2$ and arylaldoximes afforded [$PtCl_2$(PPh_3){N(OH)=CHAr}].
- *cis,trans* and/or *(E),(Z)*-isomers equilibria were studied in solution.
- [$PtCl_2$(PPh_3){N(OH)=CHAr}] reacted with $NaOH_{(aq)}$ under PTC conditions.
- dinuclear [Pt{μ-(κ^2-N,O)}-{N(O)=CHAr}Cl(PPh_3)]$_2$ were obtained from cis-(Z)-isomers.