Journal of Organometallic Chemistry 694 (2009) 2467–2475

Contents lists available at ScienceDirect

Journal of Organometallic Chemistry

journal homepage: www.elsevier.com/locate/jorganchem

Cyclometallated platinum(II) compounds with imine ligands derived from amino acids: Synthesis and oxidative addition reactions

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ARTICLE INFO

Article history:
Received 31 March 2009
Received in revised form 16 April 2009
Accepted 17 April 2009
Available online 3 May 2009

Keywords:
Platinum
Imine
Amino acid
Chirality
Oxidative addition
Cyclometallation

ABSTRACT

The reactions of $[PtMe_2(\mu\text{-}SMe_2)]_2$ with imines 4-$ClC_6H_4CH{=}NCHRCO_2Me$ (R = H (**1a**), Me (**1b**), ^{i}Pr (**1c**), $CH_2C_6H_4$(4'-OH) (**1d**), C_6H_5 (**1e**), $CH_2C_6H_5$(**1f**)) derived from natural amino acids produced under mild conditions cyclometallated platinum(II) compounds $[PtMe\{\kappa^2\text{-}(C,N)\text{-}4\text{-}ClC_6H_3CH{=}NCHRCO_2Me\}(SMe_2)]$ (**2a–2f**). These compounds gave the corresponding phosphine derivatives $[PtMe\{\kappa^2\text{-}(C,N)\text{-}4\text{-}ClC_6H_3CH{=}NCHRCO_2Me\}(PPh_3)]$ (**3a–3f**). The corresponding cyclometallated platinum(IV) compounds $[PtMe_2I\{\kappa^2\text{-}(C,N)\text{-}4\text{-}ClC_6H_3CH{=}NCHRCO_2Me\}(PPh_3)]$ (**4**) arising from intermolecular oxidative addition of methyl iodide were obtained with a high degree of stereo selectivity. Analogous results were obtained for imine 2,6-$Cl_2C_6H_3CH{=}NCH(CH_2C_6H_5)CO_2Me$ (**1g**) in a process involving intramolecular oxidative addition of a C–Cl bond. The obtained compounds were fully characterized including structure determinations for compounds **3f**, **4d** and **4f**.

1. Introduction

There is growing interest in the synthesis, reactivity and applications of organometallic complexes with biologically important ligands, in particular α-amino acids and their derivatives are highly versatile ligands in this field. Several examples of cyclopalladated compounds with ligands derived from amino acids have been reported [1] while platinum analogues have been less explored [2]. In addition, compared to the reported examples of platinum(II) complexes with amino acid derivatives as ligands, there are much fewer examples of platinum(IV) complexes in spite of the biological activity of the latter [3].

On the other hand, studies concerning oxidative addition of alkyl halides to chiral-at-ligand platinum(II) planar complexes have been reported [4] and the potential stereo selectivity of this process is relevant in asymmetric catalysis.

The aim of this work is to prepare cyclometallated platinum(II) compounds with imine ligands derived from methyl esters of natural amino acids and to study the oxidative addition of methyl iodide to such compounds in order to obtain the corresponding platinum(IV) derivatives.

2. Results and discussion

Imines **1a**–**1d** were prepared following an analogous procedure to that reported in the literature [5] while imines **1e**–**1g** were prepared as reported [1a] (see Table 1). As shown in Scheme 1, the cycloplatination reaction of imines **1a**–**1f** was carried out using $[PtMe_2(\mu\text{-}SMe_2)]_2$ as precursor and the conditions reported in the literature [6]. The process involves activation of a C–H bond followed by methane elimination and leads to formation of platinum(II) compounds **2a**–**2f** in high yields. Compounds **2** were characterized by elemental analyses, mass spectrometry and ^{1}H and ^{195}Pt NMR spectroscopy. All data are consistent with the structures proposed in Scheme 1 for compounds **2** in which the imine acts as a bidentate [C,N] ligand and the coordination sphere of platinum is completed with a methyl and a dimethylsulfide ligands [6]. These are coupled to platinum and the observed *J*(H-Pt) values are in the expected ranges, which are *ca.* 80 Hz for the methyl ligand and 25–30 Hz for the dimethylsulfide ligand. In addition, both the imine proton and the aromatic proton adjacent to the metallated carbon (H_1) are coupled to platinum with *J*(H–Pt) values in the range 50–55 and 66–68 Hz, respectively. In the ^{195}Pt NMR spectra, a single peak is observed in each case and the chemical shift is consistent with a platinum(II) coordinated to a [C,C,N,S] donor atoms set [7]. In all cases, the most intense peak in the mass spectra corresponds to the loss of a methyl ligand.

The reaction of compounds **2** with 1 equiv. of triphenylphosphine produced the corresponding compounds **3** in a substitution

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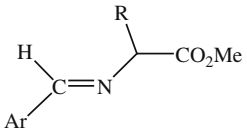
doi:10.1016/j.jorganchem.2009.04.019

Table 1
Imines studied in this work

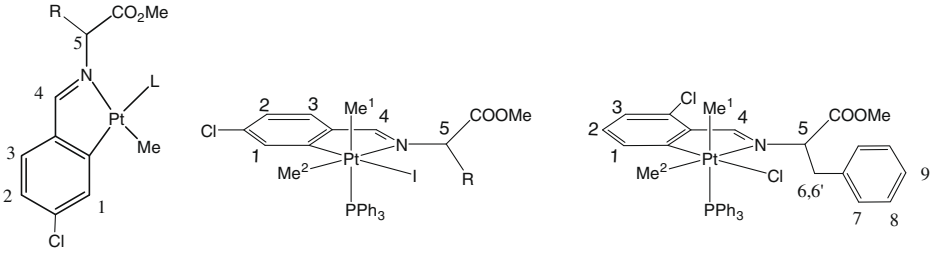
General formula:



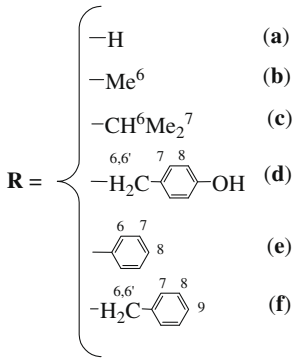
	Ar	R	Related amino acid
1a	4-ClC_6H_4	H	*Glycine*
1b	4-ClC_6H_4	Me	*Alanine*
1c	4-ClC_6H_4	$CHMe_2$	*Valine*
1d	4-ClC_6H_4	$CH_2C_6H_4$(4'-OH)	*Tyrosine*
1e	4-ClC_6H_4	C_6H_5	*Phenylglycine*
1f	4-ClC_6H_4	$CH_2C_6H_5$	*Phenylalanine*
1g	2,6-$Cl_2C_6H_3$	$CH_2C_6H_5$	*Phenylalanine*

process of the sulfide for the phosphine ligand carried out in acetone. The lower yields obtained for **3a** and **3b** might be related to the higher solubility of these compounds in diethyl ether used to isolate the products. The compounds were characterized by elemental analyses, mass spectrometry, ^1H, ^{31}P and ^{195}Pt NMR spectroscopy, and the crystal structure of **3f** was solved. The obtained data indicate that the [C,N] metallacycle is preserved in the substitution process and the coordination of the platinum(II) atom is completed with a methyl and a triphenylphosphine ligands. In the ^1H NMR spectra, in addition to signals corresponding to the coordinated PPh_3, a high field shift of the protons of both the methyl ligand and the amino ester moiety compared to compounds **2** is observed. The latter observation suggests that the aromatic rings of the phosphine ligand are close to these groups. In addition, the measured *J*(H–Pt) values for the methyl ligand and the imine proton are in the same range than those observed for compounds **2**, while the coupling to platinum decreases from 66–68 to 52–54 Hz for the aromatic proton adjacent to the metallated position. These results suggest that the triphenylphosphine is *trans* to the metallated aryl which is confirmed by the *J*(P–Pt) values in the range 2260–2290 Hz observed in both the ^{31}P and the ^{195}Pt NMR spectra [8]. The $\delta(^{195}Pt)$ values are high-field shifted upon replacement of SMe_2 for PPh_3 ligand in *ca.* 200 ppm in agreement with previous data for analogous compounds [7]. The crystal structure obtained for compound **3f** reveals total racemization of the imine ligand since it consists of a racemate. This suggests that the asymmetric carbon in the amino acid fragment is more prone to racemization than those in analogous ligands derived from *S*-α-methylbenzylamine or *R*-1-(1-naphthyl)ethylamine for which analogous platinum(II) derivatives have been obtained without evidence of racemization [9]. The higher acidity of the hydrogen bonded to the asymmetric carbon in the amino acid derivatives favours the racemization process [10] as previously observed for analogous palladium derivatives [1a].

Formation of the corresponding platinum(IV) compounds was initially attempted by intermolecular oxidative addition reaction of methyl iodide to compounds **3** (method **A** in Scheme 1). Analogous processes have been studied and shown to produce initial *trans* oxidative addition [11] followed by isomerization in such a way that the bulky triphenylphosphine is placed in a less hindered position which is perpendicular to the metallacycle plane [9]. Following this procedure platinum(IV) compounds **4a**, **4e** and **4f**, shown in Scheme 1, were obtained with high yields while the corresponding reactions for the remaining compounds led to decomposition processes. In view of these results, a "one-pot" procedure (method **B** in Scheme 1) was attempted from imines **1b**, **1c** and **1d**. This procedure gave platinum(IV) compounds **4c** and **4d** in fair yields, while formation of compound **4b** remained elusive. The only compound that could be isolated for imine **1b** following methods **A** or **B** was characterized by NMR spectra as *trans*-[PtMeI(PPh_3)$_2$] [12]. This compound was also produced from imines **1c** and **1d** using method **A**. Finally, for ligand **1g** derived from phenylalanine and containing two chloro substituents in the *ortho* positions of the aryl ring, an intramolecular oxidative addition of a C–Cl bond [13], followed by reaction with triphenylphosphine (method **C** in Scheme 1) allowed the preparation of platinum(IV) compound **4g**.



L = SMe_2 (**2**); PPh_3 (**3**) (**4**) (**4g**)



R = –H (**a**); –Me^6 (**b**); –CH^{6}Me$_2$^{7} (**c**); –H$_2$C–C$_6$H$_4$–OH (**d**); –C$_6$H$_5$ (**e**); –H$_2$C–C$_6$H$_5$ (**f**)

Scheme 1.