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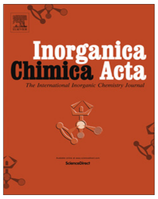

Synthesis and reactivity of thiosemicarbazone palladacycles. Crystal structure analysis and theoretical calculations

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ABSTRACT

Reaction of the thiosemicarbazones $\mathrm{3\text{-}FC_6H_4C(Me){=}NN(H)C({=}S)NHR}$, (R = Et, **a**; Ph, **b**) with potassium tetrachloropalladate(II) in ethanol, lithium tetrachloropalladate(II) in methanol or palladium(II) acetate in acetic acid gave the tetranuclear cyclometallated complexes $\mathrm{[Pd\{3\text{-}FC_6H_3C(Me){=}NN{=}C(S)NHR\}]_4}$ (**1a**, **1b**). Reaction of **1a**, **1b** with the tertiary phosphines dppm, dppe, dppp, dppb or *trans*-dppen in 1:2 M ratio gave $\mathrm{[(Pd\{3\text{-}FC_6H_3C(Me){=}NN{=}C(S)NHR\})_2(\mu\text{-}PPh_2(CH_2)_{\mathit{n}}PPh_2)]}$, ($n = 1$, **2a**–**b**; 2, **3a**–**b**; 3, **4a**–**b**; 4, **5a**–**b**), $\mathrm{[(Pd\{3\text{-}FC_6H_3C(Me){=}NN{=}C(S)NHR\})_2(\mu\text{-}PPh_2CH{=}CHPPh_2)]}$, (**6a**–**b**). Treatment of **1a**, **b** with dppm in 1:4 M ratio gave the mononuclear complexes $\mathrm{[Pd\{3\text{-}FC_6H_3C(Me){=}NN{=}C(S)NHR\}(Ph_2PCH_2PPh_2\text{-}\mathit{P})]}$ (**7a**–**b**). Reaction of the latter with an equimolar amount of $\mathrm{[PdCl_2(PhCN)_2]}$ gave $\mathrm{[PdCl_2\{Pd[3\text{-}FC_6H_3C\text{-}(Me){=}NN{=}C(S)NHR](PPh_2CH_2PPh_2)\text{-}\mathit{P,S}\}]}$, (**8a**–**b**). The molecular structure of ligands **a** and **b**, and of complex **6a** have been determined by X-ray diffraction analysis. The ligands and complexes have also been characterized by Density Functional Theory (DFT) calculations in order to obtain structural information for the species for which no X-ray data were available.

1. Introduction

Thiosemicarbazones are very interesting ligands due to the varied properties they possess such as potential antitumoral, antimicrobial, and antifungal drugs as well as analytical reagents to determine, fix and entrap heavy metal ions [1–6]. Both biological activity and analytical properties are closely associated to their complexing ability, to their reactivity enhancement after coordination and to a tendency to take part in template reactions on matrices of transition metal ions [7–12]. The subsequent reactions are controlled by the structural features as ligands, the nature of substituents, the arrangement and space orientation of their complexing groups, and the mutual effect of ligands in the metal coordination sphere.

Thiosemicarbazones usually coordinate to the metal through the imine nitrogen and the sulfur atom [13,14], although there are ligands with more than two donors, the number of which depends on the aldehyde or ketone, and on the tautomeric equilibrium of the thiosemicarbazone [15,16]; more often than not sulfur coordinates in the thiolic form [13–16,1,17]. In thiosemicarbazone palladacycles the organic ligand binds tightly to the metal as terdentate [*C*,*N*,*S*] in a tetranuclear [18] structure through $\mathrm{Pd{-}S_{chelating}}$ and $\mathrm{Pd{-}S_{bridging}}$ bonds. The strength of the former bond is put forward in the reactivity of the palladacycles with nucleophiles, where even treatment with strong chelating tertiary diphosphines yields complexes with the ligand in a [*C*,*N*,*S*] fashion and a mono-coordinated diphosphine; the ensuing complexes perform as [*P*,*S*] metalloligands.

Herein, we report the synthesis and reactivity of 3-fluorinated thiosemicarbazone palladacycles: the initial tetranuclear complexes bearing the two-fused chelate ring system at palladium [19–26] were treated with tertiary diphosphines to yield new mononuclear and dinuclear metallacycles as a function of the applied molar ratio. The former species behave as metalloligands and they are the starting materials for the preparation of new bimetallics. Structural information for those substances where crystal structure analysis was not possible was obtained from DFT calculations.

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2. Results and discussion

Although the compounds depicted hererin are similar to others reported by us [18,19,22,26,27] we sought to carry out DFT calculations in order to complement the diffractometric analysis when this is not possible, thus substantiating the suggested structures on the sole basis of spectroscopic data.

Thiosemicarbazones **a** and **b** were prepared by reaction of 4-ethyl-3-thiosemicarbazide and 4-phenyl-3-thiosemicarbazide with 3′-fluoroacetophenone, which were fully characterized (see Section 7). The NHR and NH groups gave rise to characteristic *v* (N—H) bands in the IR spectra *ca.* 3350 and 3250 cm^{-1}, the latter disappeared in the spectra of the complexes; the typical *v*(C═N) and *v*(C═S) stretches appeared in the ranges 1604–1599 and 812–785 cm^{-1}, respectively. The ^1H NMR spectra showed signals *ca.* 8.60 (**a**), 9.35 (**b**) ppm and 7.55 (**a**), 8.79 (**b**) ppm for the N*H* and N*H*R protons, respectively. Reaction of **a**–**b** by any one of the three alternative methods described, *i.e.*, potassium tetrachloropalladate in ethanol (method 1); lithium tetrachloropalladate in methanol (method 2); or palladium(II) acetate in glacial acetic acid (method 3), resulted in all cases in the tetranuclear species, [Pd{3-$FC_6H_3C(Me){=}NN{=}C(S)NHR$}]$_4$ (R = Et **1a**, R = Ph **1b**), as air-stable solids, with the ligand in the *E*,*Z* configuration, which were fully characterized by microanalytical, mass spectra, IR and ^1H NMR determinations (see Section 7). The mass spectrum (FAB) showed peaks at *m*/*z* 1375 (**1a**) and 1567 (**1b**) for the molecular ion whose isotopic composition suggests a tetranuclear complex of formula $C_{44}H_{48}F_4N_{12}Pd_4S_4$ (**1a**) and $C_{60}H_{48}F_4N_{12}Pd_4S_4$ (**1b**) (see Section 7). The *v*(C═N) band was shifted to lower wavenumbers upon complex formation by *ca.* 41 cm^{-1} [27] indicating palladium coordination to the C═N moiety through the nitrogen lone pair [28,29]. The absence of the N*H* resonance in the ^1H NMR spectra indicated deprotonation of the —NH— group [30,31], with loss of the C═S double bond character as confirmed by the absence of the *v*(C═S) band; this has been confirmed by the crystal structure resolution of complex **6a** (*vide infra*).

Metallation of the ligands was also made clear from the absence of the four proton spin system ABCD of the substituted phenyl ring; in the spectra of the complexes only three resonances were observed, inclusive of the coupling to the ^{19}F nucleus, where appropriate, which were unambiguously assigned to the H2, H4 and H5 protons (see Section 7).

3. Reactivity of the complexes

Treatment of **1a** and **1b** with the corresponding diphosphine dppm, dppe, dppp, dppb or *trans*-dppen [32] in 1:2 M ratio gave the dinuclear palladacycles [(Pd{3-$FC_6H_3C(Me){=}NN{=}C(S)NHR$})$_2$(μ-$Ph_2P(CH_2)_nPPh_2$)], (*n* = 1, **2a**–**b**; 2, **3a**–**b**; 3, **4a**–**b**; 4, **5a**–**b**), [(Pd{3-$FC_6H_3C(Me){=}NN{=}C(S)NHR$})$_2$(μ-$Ph_2PCH{=}CHPPh_2$)], (**6a**–**b**), with a bridging phosphine ligand, as pure air-stable solids, which were fully characterized (see Scheme 1 and Section 7).

The symmetric nature of the complexes was evident from the ^1H NMR spectra, which showed only one set of signals; consequently, only one singlet was observed in the ^{31}P–{^1H} spectra showing two equivalent phosphorus nuclei; with a chemical shift value pointing towards a phosphorus *trans* to nitrogen geometry [33–35]. The ^1H NMR spectra showed the H5 resonance was coupled to the ^{31}P nucleus and shifted to lower frequency between 0.9 and 1.4 ppm, suggesting a P *trans* to N arrangement [36].

Reaction of **1a**–**b** with the short-bite diphosphine $Ph_2PCH_2PPh_2$ (dppm) in 1:4 M ratio gave complexes [Pd{3-$FC_6H_3C(Me){=}NN{=}C(S)NHR$}($Ph_2PCH_2PPh_2$-*P*)] **7a**–**b** (Scheme 1), as pure air-stable compounds. Characteristic microanalytical and spectroscopic data are given in the Section 7. The mononuclear compounds showed cleavage of only the Pd—$S_{bridging}$ bond with coordination of the phosphine through only one phosphorus donor.

In the ^{31}P–{^1H} spectra two doublets were assigned to the two non-equivalent phosphorus nuclei with the signal for the phosphorus nucleus bonded to the metal center at higher frequency. The proton part of the *PCH₂P* ABXY spin system appeared as an apparent doublet *ca.* 3.3 ppm.

Treatment of **7a**–**b** with an equimolar amount of [$PdCl_2(PhCN)_2$] gave the homobimetallics [$PdCl_2${Pd[3-$FC_6H_3C(Me){=}NN{=}C(S)NHR$]($PPh_2CH_2PPh_2$)-*P*,*S*}], **8a**–**b**, as pure air-stable solids, which were completely characterized (see Scheme 1 and Section 7). The analytical and spectroscopic data showed that the second metal was bonded *via* the phosphorus and sulfur atoms in a dimetallic six-membered chelate ring. Important spectroscopic features of **8a**–**b** include two *v*(Pd—Cl) bands in the IR spectra, with that *trans* to the phosphorus atom appearing at lower wavelengths, *ca.* 287 cm^{-1}, in agreement with the greater *trans* influence of the phosphorus atom, and the Pd—Cl stretch *trans* to sulfur at *ca.* 326 cm^{-1}. The ^{31}P NMR spectra showed the low-field shift of the terminal ^{31}P resonance upon coordination to the metal, which was displaced by *ca.* 44 ppm, appearing at *ca.* 17 ppm, whilst the signal of the initially coordinated phosphorus atom shows a negligible shift. The resonance for the PCH_2P protons, part of the *PP′HH′* system, appeared as an apparent triplet *ca.* 3.25 ppm, with an *N* value of 23 Hz (see the Section 7).

4. Structural studies: crystal structures of ligands a and b, and complex 6a

Suitable crystals were grown by slowly evaporating chloroform/*n*-hexane solutions. The crystal structures and the labelling schemes are shown in Figs. 1 and 2; crystal data are given in Table 1.

4.1. Crystal structures of 3-$FC_6H_4C(Me){=}NN(H)C({=}S)NHEt$ (a) and 3-$FC_6H_4C(Me){=}NN(H)C({=}S)NHPh$ (b)

Ligands **a** and **b** (Fig. 1) crystallize in the triclinic $P\bar{1}$ space group as the *E*-isomer with respect to the N(1)—C(7) bond and *Z* with respect to the N(3)—C(8) bond. This arrangement is often found in thiosemicarbazones with at least one hydrogen attached to N(3) [38,39] due to weak N(3)—H(3)···N(1) hydrogen bonding. The C(8)—S(1), 1.622(16) Å (**a**) and 1.6733(17) Å (**b**), and the N(1)—C(7), 1.280(2) Å (**a**) and 1.284(2) Å (**b**), bond distances are consistent with a formal double bond character. The C(1)—C(7)—N(1) 115.86(14)° (**a**), 115.50(14)° (**b**), and C(7)—N(1)—N(2) 119.44(14)° (**a**), 118.87(14)° (**b**), bond angles are in agreement with sp^2 hybridization of the carbon and nitrogen atoms. The thioamide chain C(7)—N(1)—N(2)—C(8)—S(1)—N(3) is planar (rms = 0.0091 **a** and 0.0251 **b**) and at an angle of 9.83(9)° **a**, and 13.53(13)°, **b** with the fluorinated phenyl ring (rms = 0.0072, **a** and 0.0035, **b**). The parameters for the hydrogen bonding interaction in **a** (Fig. S1, SI) and **b** (Fig. S2, SI), are as follows: **a**, N(3)···N(1) 2.5957(19) Å, H(3 N)···N(1) 2.20 Å, N(3)—H(3 N)···N(1) 108.2°, N(2)···S(1)#1 3.627 Å, H(2 N)···S(1)#1 2.772 Å, N(2)—H(2 N)···S(1)#1 172.70°; S(1)···C(11)#1 3.437(2) Å, H(11C)#1···S(1) 2.62 Å, C(11)#1—H(11C)#1···S(1) 142.8°, with the symmetry operation #1[−*x*, −*y*, −*z*]; and N(3)···F(1)#2 3.2416(18) Å, H(3 N)···F(1)#2 2.610 Å, N(3)—H(3 N)···F(1)#2 131.22°, with the symmetry operation #2 [−*x* − 1, −*y*, −*z* + 1]. The implication of the fluorine atom can explain the *endo* disposition of the ligand in the solid state; **b**, N(3)···N(1) 2.5878(19) Å, H(3)···N(1) 2.158 Å, N(3)—H(3)···N(1) 110.53°, N(2)···S(1)#1 3.7840 Å, H(2)···S(1)#1 2.925 Å, N(2)—H(2)···S(1)#1 176.32°; S(1)···C(15)#1 3.4690(19) Å,