

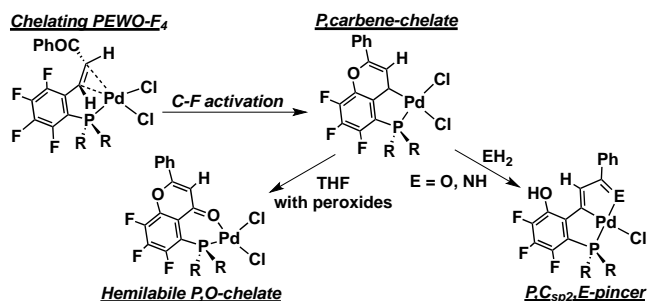
## Reactivity of Fluorinated-Chalcone Phosphines, RPEWO-F<sub>4</sub>, Induced by C–F Activation upon Coordination to PdCl<sub>2</sub>.

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**ABSTRACT:** The phosphines *E*-PR<sub>2</sub>(*o*-C<sub>6</sub>F<sub>4</sub>-CH=CH-C(O)Ph) (R = Ph, *o*-Tol, Cy) ligands, abbreviated as RPEWO-F<sub>4</sub>, are stable in solution, but they develop a rich reactivity when coordinated to PdCl<sub>2</sub>. The chelate P-olefin coordination to PdCl<sub>2</sub> leads eventually to a *Z* conformation of the fluorinated-chalcone group *o*-C<sub>6</sub>F<sub>4</sub>-CH=CH-C(O)Ph. From there, a cyclization reaction occurs involving the C=O group and activation of a F atom, yielding a strongly chelated PdCl<sub>2</sub>(P-carbene) complex. The carbene carbon atom in the complex displays some electrophilicity, which is expressed in hydrolysis, ammonolysis, and oxidation (with peroxide) reactions, affording PdCl<sub>2</sub> complexes with new P,C,O-pincer, P,C,N-pincer, or P,O-chelate fluorinated ligands. The C–F activation reactions are slow compared to the catalysis rates when the [PdCl<sub>2</sub>(RPEWO-F<sub>4</sub>)] complexes have been used in Negishi catalyses. Consequently, the reactivity discussed here is not expected to interfere with the interpretation of the data obtained in Pd-catalytic studies or processes, at least for fast transmetalating nucleophiles.



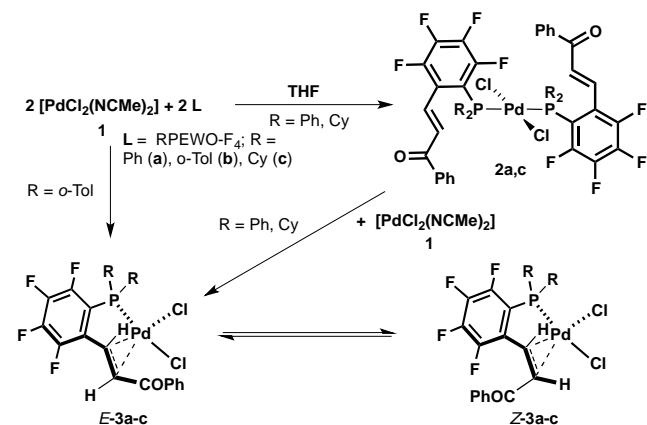
### INTRODUCTION

Recently we have been studying the *in situ* formation of complexes [PdCl<sub>2</sub>(RPEWO-F<sub>4</sub>-chel)] (**3a-c**), from [PdCl<sub>2</sub>(NCMe)<sub>2</sub>] (**1**) and the corresponding PEWO ligand PR<sub>2</sub>(EWO) where R = Ph (**a**), *o*-Tol(**b**), Cy (**c**) and EWO is a fluorinated chalcone fragment (Scheme 1).<sup>1</sup> These complexes are good precatalysts for Negishi reactions. The PEWO ligands are remarkably efficient in the reductive elimination step of the catalytic cycle and, in Pd-catalyzed aryl–alkyl reactions, they suppress undesired "reductions" to ArH + olefin.<sup>2</sup> The PEWO ligands are able to carry out fast Me–Me coupling at –30 °C. Also, they induce C<sub>6</sub>F<sub>5</sub>–C<sub>6</sub>F<sub>5</sub> coupling from *cis*-[Pd(C<sub>6</sub>F<sub>5</sub>)<sub>2</sub>(THF)<sub>2</sub>] at 25 °C as fast as the very efficient P<sup>t</sup>Bu<sub>3</sub> or <sup>t</sup>BuXphos ligands do.<sup>3,4</sup>

In our recent study we found that *trans*-[PdCl<sub>2</sub>(*E*-RPEWO-F<sub>4</sub>-monodent)<sub>2</sub>] (**2a,c**) complexes with *E*-configuration at the double bond are intermediates in the course of the reaction of the PdCl<sub>2</sub> synthon with the *E*-PEWO ligands towards [PdCl<sub>2</sub>(RPEWO-F<sub>4</sub>-chel)] (**3a-c**). The final chelated complexes **3a-c** display *E/Z* configurational equilibria with equilibrium constants depending on the solvent and on R.<sup>1</sup> The rate of this configurational change is moderate (it takes some hours at room temperature), although very fast compared to conventional olefins, and requires olefin decoordination. The comparatively low values of the configurational isomerization barriers in **3a-c** are due to the fact that the third P-substituent (the EWO fragment) is a fluorinated chalcone and the polarization of the C=C bond towards both extremes, induced by the

F substituents in the aryl and the C=O group, makes the olefin an electron deficient one (EDO) with an unusually low rotational barrier. Consistently, the C=C bond behaves as a strongly electron withdrawing olefin (EWO) when coordinated to a metal center.<sup>1,2,3</sup> Chalcones (benzylidene acetophenones) are molecules of high pharmacological,<sup>5</sup> biological,<sup>6</sup> and photo-physical interest.<sup>7</sup>

**Scheme 1.** Synthesis of complexes *E*-**3a-c** and *Z*-**3a-c**.



Here we report the new types of chelate PdCl<sub>2</sub> complexes with fluorinated phosphines derived from **3a-c**, which are formed

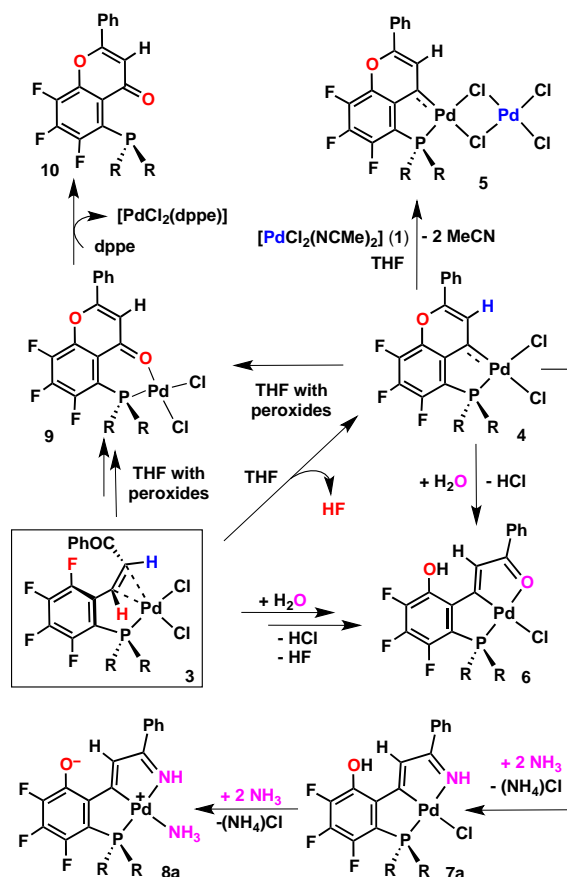
because the reactivity of a C–F bond in the chalcone fragment is enhanced when the phosphine is coordinated to PdCl<sub>2</sub>.

## RESULTS AND DISCUSSION

*Synthesis of [PdCl<sub>2</sub>(RP-carbene)] complexes from 3a-c.* Ligand CyPEWO-F<sub>4</sub> (**c**) is particularly reactive and its evolution in freshly distilled THF (Scheme 1) does not cease at the detected [PdCl<sub>2</sub>{Z-(CyPEWO-F<sub>4</sub>)}] (**Z-3c**), but continues to give quantitatively, after some time, an orange-reddish product [PdCl<sub>2</sub>(CyP-carbene)] (**4c**), which was isolated and fully characterized.<sup>8</sup> The Ph and *o*-Tol analogues (**4a** and **4b** respectively) are also formed quantitatively, but at much slower paces. The rates of this transformation follow the trend Cy >> Ph >> *o*-Tol (details in supporting information).

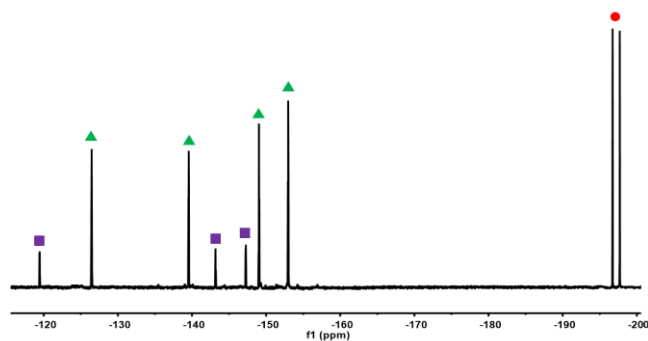
The syntheses of **4** and the rest of compounds reported in this work are summarized in Scheme 2. The numeric labels stand for the cases of the three ligands (**a-c**) unless otherwise specified.

**Scheme 2.** Reactivity of **3a-c** complexes



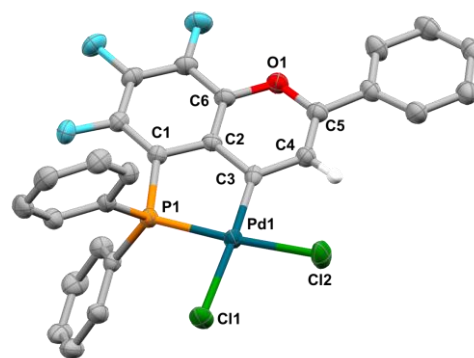
The [PdCl<sub>2</sub>(RP-carbene)] complexes **4** arise from loss of the F and H atoms highlighted in red in Scheme 2:<sup>9</sup> a cyclization initiated by nucleophilic attack of the acyl oxygen of **3** to the closest C–F carbon atom leads eventually to formation of the [PdCl<sub>2</sub>(RP-carbene)] complexes **4**. The HF formed is clearly seen as a doublet (red dot,  $\delta = 197.22$  ppm,  $^1J = 455$  Hz) in the <sup>19</sup>F NMR spectra of the reaction mixtures (Figure 1 for the case of **4a**).<sup>10</sup> The signals of the still unreacted **Z-3a** (green triangles) and the [PdCl<sub>2</sub>(PhP-carbene)] product **4a** (purple squares) are observed in the course of the process. The signals

of **4a** are small relative to HF because the spectrum was recorded when most **4a** formed had precipitated due to its low solubility.



**Figure 1.** <sup>19</sup>F NMR spectrum of a solution of **Z-3a** in freshly distilled THF, after 1 day at room temperature. Four non-equivalent F atoms of **Z-3a**, three non-equivalent atoms of **4a**, and HF are observed.

The X-Ray structure of **4a** is displayed in Figure 2, The C6–O1–C5 angle is 119.7(4)° and the C3–C4, C4–C5, and C5–O1 bond distances have values in between simple and double bonds. The six-membered heterocycle is perfectly flat and coplanar with the fluorinated aryl ring, supporting effective electron delocalization within the fragment and aromatic stabilization of the carbene.<sup>11</sup> This fragment makes a dihedral angle of only 5.8° with the pendant phenyl group.

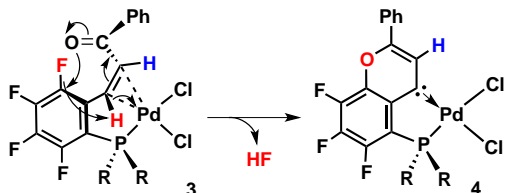


**Figure 2.** X-Ray structure of **4a**. Hydrogen atoms are omitted for clarity. Selected bond lengths (Å): Pd(1)–P(1) = 2.2206(11); Pd(1)–C(3) = 1.935(5); Pd(1)–Cl(1) = 2.3461(13); Pd(1)–Cl(2) = 2.3689(13); C(2)–C(3) = 1.475(6); C(3)–C(4) = 1.409(6); C(4)–C(5) = 1.370(7); C(5)–O(1) = 1.349(6); O(1)–C(6) = 1.369(5); C(6)–C(2) = 1.381(6).

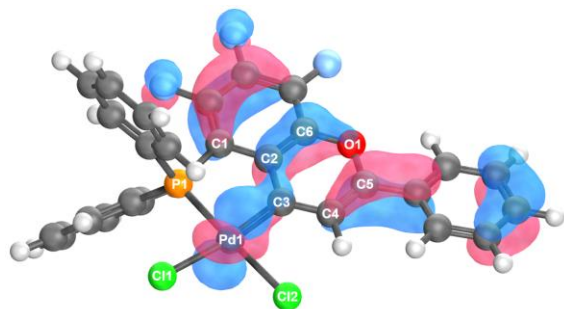
The nucleophilic attack giving rise to **4** is not observed on the free RPEWO-F<sub>4</sub> ligands, suggesting that the C–F reactivity requires enhancement upon chelate coordination to PdCl<sub>2</sub>. This is a reasonable assumption since both the coordination of P and the coordination of the double bond should result in reduction of electron density on the C(aryl) atoms. The *Z* conformation of the olefin and the angular coordination of the double bond relative to the Pd coordination plane impose that the leaving F and the H atom eventually forming HF (in red in Scheme 3) are situated at the aryl side opposite to the one

undergoing the nucleophilic attack by oxygen.<sup>6,7b</sup> The overall process of making and breaking these bonds might be concerted.

**Scheme 3.** Proposed mechanism of formation of the chelate P-carbene complexes **4**. The carbene nature of C3 is highlighted.



Clearly, the simple Lewis proposal of double and single bonds used for **4** in Schemes 2 and 3 is just a naïve representation. However, it is not useful either to be proposing several simple resonant forms for **4** or for other complexes at each point of this work: it would be cumbersome to do this. Let's then just keep in mind for the discussions to come that the proposed extended aromaticity of the system is supported by the high delocalization of several full or empty molecular orbitals, and the electron density in the fragments chelating the Pd atom is quite polarizable along the successive reactions. The DFT optimized geometry of **4a** (wb97xd level) matches perfectly the X-Ray structure, also in the practically coplanar arrangement of the three six-membered rings. The molecular structures of the *o*-Tol and Cy analogs are very similar (see Figures S4 and S5), so the conclusions for **4a** must be reasonably valid for the three cases. Figure 3 shows, as an example, one of the occupied molecular orbitals (HOMO-16), which is involving all carbon atoms of the tricyclic fragment of **4a** and, in addition, the Pd atom, leading to Pd1–C3  $\pi$  interaction (in this respect see later entry 1 in Table 1).



**Figure 3.** Example of an occupied MO (HOMO-16).

Natural Bond Order (NBO) and Second-Order Perturbation Theory (SOPT) analysis was applied to complex [PdCl<sub>2</sub>(PhP-carbene)] (**4a**).<sup>12</sup> The results of the SOPT analysis, summarized in Table 1, collect selected data of the main electron donations involving the ring where the "empty" p orbital of the carbene carbon atom (C3) is implicated, as well as the composition of the orbitals involved. Entries 1-3 are donations to the empty p orbital of the carbene carbon atom (labeled LV C3). The strongest donor (entry 2) is the C4–C5 bonding orbital **BD C4–C5**, containing 100% p electron density. This donation is larger than any of the two other important interactions involving LV C3 as acceptor: the one in entry 3, which proceeds from the C2–C6 bonding orbital **BD C2–C6** (also 100% p density), and the one in entry 1, which comes from a **LP Pd1** 100% d<sub>z</sub> corresponding to Pd (Figure S11). In fact entry 1 is what we usually call Pd-backdonation to the carbene carbon atom (see

also Figure 3), and we can see that, in spite of the high SOPT energy associated to this donation, it only represents less than 20% of the total electron transfer to this the carbene C3 atom. On the other hand, the C4–C5 and C2–C6 **BD\*** antibonding orbitals receive donation from the lone pairs of the oxygen atom O1 (entries 4 and 5), confirming the participation of O1 in the proposed aromaticity of the system.

**Table 1.** Selected Donor-Acceptor interactions and SOPT energies (kcal mol<sup>-1</sup>) for **4a**. The atom labels are as for the X-Ray structure in Figure 2.

Entry	Donor/Contribution	Acceptor/Contribution	Energy
1	<b>LP Pd1</b> / Pd1 d	<b>LV C3</b> / C3 p	40.0
2	<b>BD C4–C5</b> / 56% C4 p, 44% C5 p	<b>LV C3</b> / C3 p	108.5
3	<b>BD C2–C6</b> / 51% C2 p, 49% C6 p	<b>LV C3</b> / C3 p	60.0
4	<b>LP O1</b> / O1 p	<b>BD* C4–C5</b> / 44% C4 p, 56% C5 p	46.5
5	<b>LP O1</b> / O1 p	<b>BD* C2–C6</b> / 49% C2 p, 51% C6 p	40.4

BD, LP and LV stand for Bonding, Lone Pair and Low Vacancy orbitals, respectively. Asterisks denote antibonding NBO orbitals. Note that p and d are always 100% contribution.

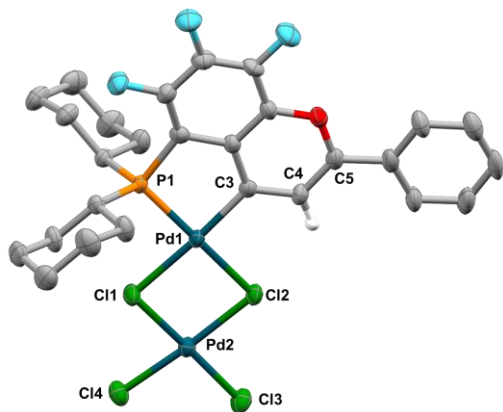
In the related X-ray structures, the change of R = Ph for the better donors R = *o*-Tol, Cy produces larger Pd–C3 bond lengths (see 1.935(5) Å in **4a**, Figure 2; 1.973(3) Å in **4b**, Figure S4; and 1.965(4) Å in **4c**, Figure S5), with almost negligible variations of the Pd–P bond lengths (2.2206(11), 2.2366(9), and 2.2244(11) Å, respectively, for **4a**, **4b**, and **4c**). However, these bond length differences become much smaller for the optimized molecular structures in the gas phase, suggesting that they are consequence of packing. In other words, for the isolated molecule the purely electronic effect of the R groups on the Pd–C3 bond turns out to be small, which is in keeping with the results of the SOPT analysis of **4a** and the relatively small bond contribution of Pd-to-C3  $\pi$  back-donation compared to C3-to-Pd  $\sigma$ -donation. This interpretation is also consistent with the fact that the  $\pi$ -interactions of C3 as acceptor center are expected to be strongly dominated by its implication with the aromatic fragment and only more modestly with the Pd atom.

In the <sup>1</sup>H NMR spectra of complexes **4**, the C4–H hydrogen atoms show unusually high chemical shifts to low field ( $\delta$  = 10.32 ppm for **4a**), which can be explained by the considerable electron donation from C4–C5 to C3 (entry 2). Obviously the high electronegativity of the two Cl substituents on Pd also helps to make C3 a stronger acceptor.<sup>13</sup> Overall the "empty" carbene p orbital achieves a calculated occupancy of 0.68 e<sup>-</sup>, which keeps a still high potential for C3 to display electrophilic behavior and reactivity.

*Reactivity of the [PdCl<sub>2</sub>(RP-carbene)] complexes.*

*a) Formation of zwitterionic complexes.* The stoichiometric reaction of **4a-c** with the precursor [PdCl<sub>2</sub>(NCMe<sub>2</sub>)] (**1**) produces quantitatively the dinuclear zwitterionic complexes [Cl<sub>2</sub>Pd( $\mu$ -Cl)<sub>2</sub>Pd(RP-carbene)] (**5a-c**). Their low solubility prevents NMR characterisation but, elemental analyses, and the X-Ray diffraction structures of **5b** (Figure S6) and **5c** (Figure 4) confirm their nature. The structures show typical square planar geometry for the palladium centers and no sig-

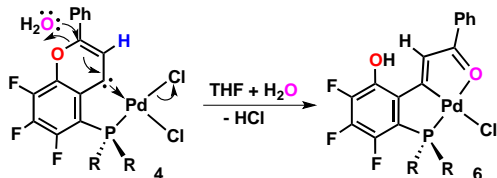
nificant variation of the Pd–C3 bond length (e.g. 1.973(3) Å in **4b** vs. 1.978(5) Å in **5b**).



**Figure 4.** X-Ray structure of **5c**. Only one of the two slightly different molecules of the asymmetric unit is shown. Hydrogen atoms and crystallization solvent molecules are omitted for clarity. The distances in the ligand are very similar to the ones detailed for **4a**. Selected bond lengths (Å): Pd(1)–P(1) = 2.2269(13); Pd(1)–C(3) = 1.982(4); Pd(1)–Cl(1) = 2.3845(12); Pd(1)–Cl(2) = 2.4117(12); C(3)–C(4) = 1.385(6); C(4)–C(5) = 1.378(6); Pd(2)–Cl(1) = 2.3299(14); Pd(2)–Cl(2) = 2.3526(12); Pd(2)–Cl(3) = 2.2628(14); Pd(2)–Cl(4) = 2.2693(13).

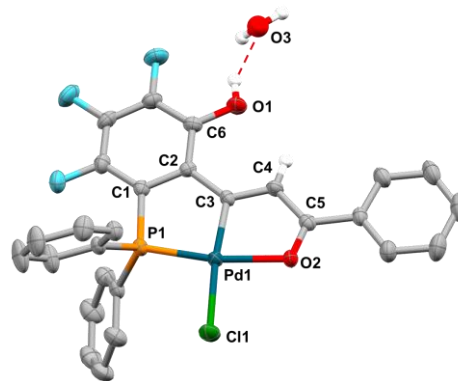
*b) Hydrolytic ring opening.* This reaction was accidentally discovered in an attempt to obtain single crystals of **4c** from  $\text{CHCl}_3/n$ -hexane. The crystals obtained were shown to contain **4c+6c** as the repetitive unit (Figure S7). The structure of **6c**, named [PdCl(CyP,C,O-pincer)] suggested a reaction with  $\text{OH}_2$  in the solvent, which could be promoted (indistinctly from **3a-c** or from **4a-c**) using THF wetted on purpose (Scheme 2). Strong kinetic dependence on water concentration, and rate influence of the R group (Cy  $\gg$  Ph  $\gg$  *o*-Tol), were observed. Scheme 4 shows the proposed mechanism of this transformation, which is triggered by nucleophilic attack by water inducing ring opening at the cyclic ether. The oxygen originally in the cycle ends up as OH in the fluorinated aryl, and the oxygen originally in the water molecule becomes the ketone oxygen replacing a dissociated  $\text{Cl}^-$  in the Pd coordination plane. Although alternative  $\text{OH}_2$  attack to the fluorinated aryl group splitting the other C–O bond would yield the same product, the related reactions with  $\text{NH}_3$  discussed below supports the former proposal. The chemoselectivity of the attack strongly points to the electron-deficiency of the carbene carbon as the driving force leading to its transformation into an electron rich vinyl carbon.

**Scheme 4.** Ring opening hydrolysis of complexes **4**.



The X-ray diffraction structure of complex **6a** is shown in Figure 5 and displays, as expected a  $\text{P,C}_{\text{sp}^2}\text{,O}$ -pincer bonding. As far as we know, there are three other reported examples of palladium complexes with  $\text{P,C,O}$ -pincer ligands. Two of them

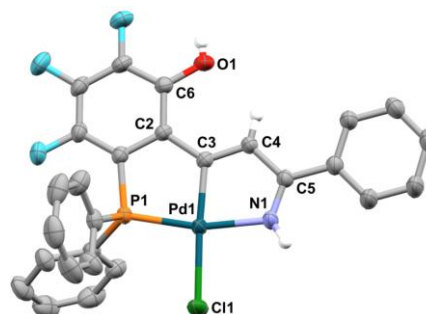
are  $\text{P,C}_{\text{aryl}}\text{,O}$ .<sup>14,15</sup> The third example, reported by our group, is a  $\text{P,C}_{\text{sp}^3}\text{,O}$ -pincer formed in an aryl migratory insertion on a PdPEWO complex.<sup>16</sup> Usually these complexes behave in Pd as hemilabile chelates that easily dissociate the oxygen atom.<sup>15</sup>



**Figure 5.** X-Ray structure of **6a**. Hydrogen atoms and crystallization solvent molecules are omitted for clarity. Selected bond lengths (Å): Pd(1)–P(1) = 2.1910(10); Pd(1)–C(3) = 1.981(4); Pd(1)–Cl(1) = 2.3821(10); Pd(1)–O(2) = 2.108(2); C(2)–C(6) = 1.412(5); C(2)–C(3) = 1.463(5); C(3)–C(4) = 1.356(5); C(4)–C(5) = 1.450(7); C(5)–O(2) = 1.259(4).

The structure observed for the [PdCl(PhP,C,O-pincer)] (**6a**) supports the assignment of C3 as a vinyl carbon (C3–C4 = 1.356 Å), and O1 as a ketone oxygen (C5–O1 = 1.259 Å). The OH group of these compounds (see specific X-ray structures in supporting information) show a strong tendency to get involved in hydrogen bonding with different H acceptors. For instance, interactions with water molecules in the crystal are found in the structure of **6a**· $\text{OH}_2$  shown in Figure 5, or in the co-crystal **4c+6c**· $\text{OH}_2$  in Figure S7, whereas in **6a** (without water) an O–H...Cl bridge is observed.<sup>17</sup> Complex [PdCl(*o*-TolP,C,O-pincer)]·THF (**6b**) displays hydrogen bond to THF (Figure S9). Because of this propensity to participate in H bonding, notable differences are found in the NMR spectra of these pincer complexes, whether recorded in the presence or absence of hydrogen bond acceptors.

*c) Ammonolytic ring opening.* The reaction of  $\text{NH}_3$  (gas) also produces ring opening of the cyclic ether in **4a** (Scheme 2). In this case the position of the imino group in the corresponding product **7a** (Figure 6) provides unambiguous assignment of the direction of the ammonolysis, and supports the proposal made for the hydrolytic ring opening. Complex **7a** contains a new hemilabile  $\text{P,C}_{\text{sp}^2}\text{,N}$ -pincer ligand.

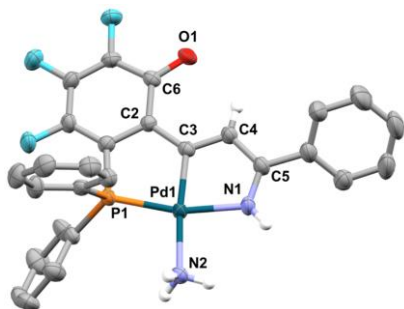


**Figure 6.** X-Ray structure of **7a**. Hydrogen atoms and crystallization solvent molecules are omitted for clarity. Selected bond lengths (Å): Pd(1)–P(1) = 2.1955(10); Pd(1)–C(3) = 1.991(4);



Pd(1)–Cl(1) = 2.3890(11); Pd(1)–N(1) = 2.062(3); C(2)–C(3) = 1.468(5); C(3)–C(4) = 1.351(5); C(4)–C(5) = 1.459(5); C(5)–N(1) = 1.292(5); C(2)–C(6) = 1.419(5); C(6)–O(1) = 1.333(5).

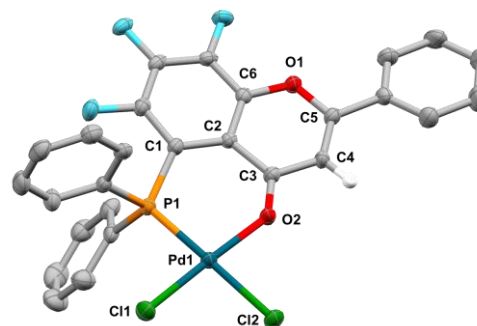
Interestingly, excess NH<sub>3</sub> is able to deprotonate the hydroxyl group of **7a** and displace the Cl<sup>−</sup> ligand forming NH<sub>4</sub>Cl and complex **8a** (see synthetic details in supporting information). Complex **8a** is formally represented in Scheme 2 as having an aryloxy group with a negative charge on oxygen, which is compensated by a positive charge on Pd. This picture highlights the zwitterionic character of **8a**. However, the structural data for **8a** (Figure 7) show that whereas the bond distances in the pincer system in **8a** are very similar to those found for **7a**, the C6–O1 distance in **8a** (1.275(4) Å) is appreciably shorter than in **7a** (1.333(5) Å), that is, closer to double bond C=O distance. This supports that the negative charge on O is in fact significantly  $\pi$  polarized towards the fluorinated aryl. A concomitant elongation of C2–C6 is also observed.



**Figure 7.** X-Ray structure of **8a**. Hydrogen atoms and crystallization solvent molecules are omitted for clarity. Selected bond lengths (Å): Pd(1)–P(1) = 2.2144(8); Pd(1)–C(3) = 2.006(3); Pd(1)–N(2) = 2.153(3); Pd(1)–N(1) = 2.066(3); C(2)–C(3) = 1.460(5); C(3)–C(4) = 1.354(5); C(4)–C(5) = 1.440(5); C(5)–N(1) = 1.297(5); C(2)–C(6) = 1.447(5); C(6)–O(1) = 1.275(4).

*d) Side transformations with peroxides in aged THF.* Although the RPEWO-F<sub>4</sub> ligands are stable in the air, all the previous reactions from **3** carried out in this work, as well as the catalysis previously reported, are carried out as routine in freshly distilled tetrahydrofuran (THF) and under N<sub>2</sub> atmosphere, using Schlenk techniques. However, in one attempt to obtain the [PdCl<sub>2</sub>{Z-(PhPEWO-F<sub>4</sub>)}] (**Z-3a**), with the reaction protocol described in Scheme 1, using as usual supposedly pure THF from an SPS apparatus (Solvent Purification System) we were surprised by the presence in the <sup>31</sup>P NMR spectrum of an unknown signal in low concentration 20 ppm upfield that of the desired product. We found that the SPS apparatus had been malfunctioning, and then we tested our suspects of presence of peroxides in that THF checking the behavior of **3a** in THF from a bottle stored in the laboratory for a long time. The quantitative formation of the new product, which precipitated as a yellow solid only sparingly soluble in THF, was observed. This species displays three non-equivalent signals in the <sup>19</sup>F NMR spectrum and was unambiguously characterized by X-Ray diffraction (Figure 8). We spare structural comments similar to the case of the other P,C,O-pincer or P-carbene complexes, which apply here also but might be tiresome for the reader. The structure of **9a** shows a [PdCl<sub>2</sub>(PhP,O-chelate)] complex and the product seems to be the result of initial formation of the carbene complex **4a** (HF is observed when starting the reaction from **3a**, as observed in Figure S3), followed

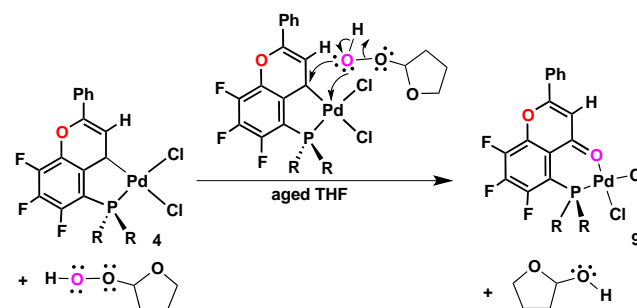
by oxidation of the carbene carbon atom to ketone. In fact, **9a** is quantitatively obtained indistinctly from **3a** or directly from **4a** (Scheme 2). The same procedure applied to **3b** yields the corresponding complex **9b**.



**Figure 8.** X-Ray structure of **9a**. Hydrogen atoms are omitted for clarity. Selected bond lengths (Å): Pd(1)–P(1) = 2.2088(6); Pd(1)–O(2) = 2.0105(16); Pd(1)–Cl(1) = 2.2668(6); Pd(1)–Cl(2) = 2.3653(6); O(2)–C(3) = 1.261(3); C(2)–C(3) = 1.457(3); C(3)–C(4) = 1.414(3); C(4)–C(5) = 1.350(3); P(1)···O(2) = 3.077.

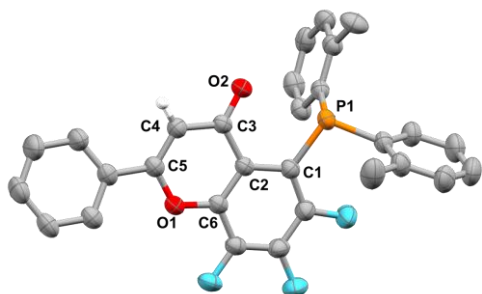
Obviously all circumstances point to peroxides in the THF acting as the oxidizing agents.<sup>18</sup> However, attempts at reproducing the synthesis with commonly used peroxides such as H<sub>2</sub>O<sub>2</sub>, *m*-CPBA, or benzoyl peroxide failed and led to oxidation of the ligand and Pd-containing decomposition products. N<sub>2</sub>O atmosphere, which has been reported to provoke insertion of O into a C(carbene)–Ir<sup>I</sup> bond,<sup>19</sup> was also tried, but it was inactive on our carbene complex. For this reason we aged on purpose a few milliliters of freshly distilled THF,<sup>20</sup> which were stored for two months under air in a Schlenk flask exposed to the sunlight. After that time, the presence of a white turbulency in the solvent could be observed, the peroxides test with KI was positive, and the 2-hydroperoxide tetrahydrofuran molecule was observed in the <sup>1</sup>H NMR spectrum (Figure S2). The aged THF was very effective. As a matter of fact, it needed to be diluted for its use (see supporting information) in order to prevent side reactions such as phosphine oxidation. The coordinated P atom is not affected under these conditions. The oxygen transfer or "insertion" should likely start by nucleophilic attack by oxygen to the electrophilic C(carbene) atom, as suggested in Scheme 5. Although we do not know for certain the reason for the selectivity of this source of peroxide, it might depend on the help of some concerted interactions in the transition state, non accessible to other peroxides.

#### Scheme 5. Synthesis of [PdCl<sub>2</sub>(RP,O-chelate)] complexes (**9**)



Finally, some attempts at displacing the new chelate ligands from their PdCl<sub>2</sub> complexes were made. Treatment of **4a,b**

with bipy or dppe failed to displace the P-carbene ligand, confirming the strong coordination of the carbene group. In contrast, dppe displaces easily the P-ketone chelate ligands **10** from complexes **9**, confirming their hemilabile behavior. These ligands could be purified by chromatography and were isolated in excellent yields. The X-ray structure of **10b** is shown in Figure 9 and makes unnecessary any further discussion about the ketone nature of the new C=O group. Comparing data of the 5-membered planar chelated palladacycle **6a**, the planar-distorted 6-membered palladacycle **9a**, and the free phosphine **10b**, both the bond lengths in Figures 5, 8 and 9, and the infrared  $\nu_{\text{CO}}$  values ( $1537\text{ cm}^{-1}$  for **6a**,  $1548\text{ cm}^{-1}$  for **9a**, and  $1639\text{ cm}^{-1}$  for **10a**), are within the ranges expected for CO bonds with significant multiplicity. The shortest CO distances and highest  $\nu_{\text{CO}}$  values are found for the free ligands.



**Figure 9.** X-Ray structure of **10b**. Hydrogen atoms are omitted for clarity. Selected bond lengths (Å): O(2)–C(3) = 1.229(3); C(2)–C(3) = 1.473(4); C(3)–C(4) = 1.444(4); C(4)–C(5) = 1.345(4); P(1)···O(2) = 2.743.

At this point we can come back to the question whether the reactivity just reported might have interfered, in an unnoted way, in the Pd catalytic studies with RPEWO- $F_4$  ligands reported so far.<sup>2,3,16</sup> A revision of our old NMR files has shown only in a few cases signals now recognized as the coordinated carbene ligands, but all these cases corresponded to unsuccessful experiments. In successful catalytic experiments there are no traces of this reactivity for reasons easy to understand: *i*) the Negishi reactions with chelate precatalysts [PdCl<sub>2</sub>{Z-(RPEWO- $F_4$ )}] are several orders of magnitude faster than the processes just discussed; and *ii*) these precatalysts will have only ephemeral existence in the presence of the ZnR<sub>2</sub> or ZnRCl nucleophiles, and will react very fast to generate [Pd<sup>II</sup>R<sub>2</sub>(RPEWO- $F_4$ -chel)], and then [Pd<sup>0</sup>(RPEWO- $F_4$ )], which is quickly oxidized by ArI to [Pd<sup>II</sup>ArI(RPEWO- $F_4$ -chel)]; *iii*) in any of these intermediates the Pd center is less acidic than in [PdCl<sub>2</sub>{Z-(RPEWO- $F_4$ )}] and the activating effect of C–F found upon coordination to PdCl<sub>2</sub>, discussed above, should be much less efficient or totally inefficient in any of them. In fact, the ligand transformations studied in this work have not had any detectable participation in our previous Negishi catalytic studies.

## CONCLUSIONS

In spite of the presence of activating C=O and C–F functions in the chalcone substituent of the phosphines *E*-RPEWO- $F_4$ , these ligands do not show any chemical evolution until their coordination to PdCl<sub>2</sub> produces [PdCl<sub>2</sub>{Z-(RPEWO- $F_4$ )}]. This coordination triggers a cyclization reaction by nucleophilic

substitution of an accessible F substituent. In this reaction, one of the C atoms of the olefin is converted into a carbene carbon coordinated to Pd.

The coordinated carbene atom still retains sufficient electrophilicity to be determinant in the chemoselective nucleophilic attack of subsequent hydrolysis and ammonolysis reactions. This residual electrophilicity is also the factor responsible for the formal insertion of O into the C(carbene)–Pd bond, upon reaction with peroxide present in aged THF solvent.

The reaction rates observed for the C–F activation reaction, which is the origin of all the complexes just discussed, are very slow compared to the catalytic rates of [PdCl<sub>2</sub>(RPEWO- $F_4$ )] complexes in Negishi catalysis, at least for the ligands with R = Ph, *o*-Tol used so far with this purpose. In spite of this, the reactivity observed here should be taken as a warning when exploring new reactions and catalysis with RPEWO- $F_4$  ligands in other conditions (*e.g.* change to other metal centers, higher temperatures, or slower (poorer) nucleophiles).

## ASSOCIATED CONTENT

### Supporting Information

Synthesis and characterization of the new complexes; X-ray diffraction structures; computational details; (PDF, 61 pages). The Supporting Information is available free of charge on the ACS Publications website.

### Notes

The authors declare no competing financial interests.

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