Synthesis, characterization and antiproliferative activity of theophylline-based Pd(II) allyl complexes

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Theophylline is a methylxantine drug used in therapy for respiratory diseases such as asthma[1] and it is constituted by two condensed heterocyclic rings bearing two nitrogens each that may be functionalized in order to obtain a wide range of compounds.[2,3]
The functionalization of both the nitrogens of the imidazole ring yields imidazolium salts that, while displaying a remarkable biological activity, are also widely used as organometallic precursors of the N-heterocyclic carbene ligands.[4]
In this abstract, we report the synthesis of theophylline-based Pd(II) allyl complexes and preliminary studies of the antiproliferative activity against A2780 and SKOV-3 human cancer cell lines.
In order to obtain these palladium complexes we have developed a synthetic route based on four steps:

1. Synthesis of theophylline derivatives by addition of alkyl bromides and K_2CO_3 to a solution of theophylline in DMF.
2. Methylation of the theophylline derivatives yielding the related imidazolium salts.[5]
3. Synthesis of Ag(I)-NHC complexes by reaction of the imidazolium salts with silver oxide.
4. One-pot reaction between the palladium precursor ($[PdCl(allyl)]_2$) and the Ag(I)-NHC complexes. In the attempt to obtain a different ligand besides to the carbene moieties, the new species (i.e. PPh_3 or isocyanides) has been added to the previous described mixture.

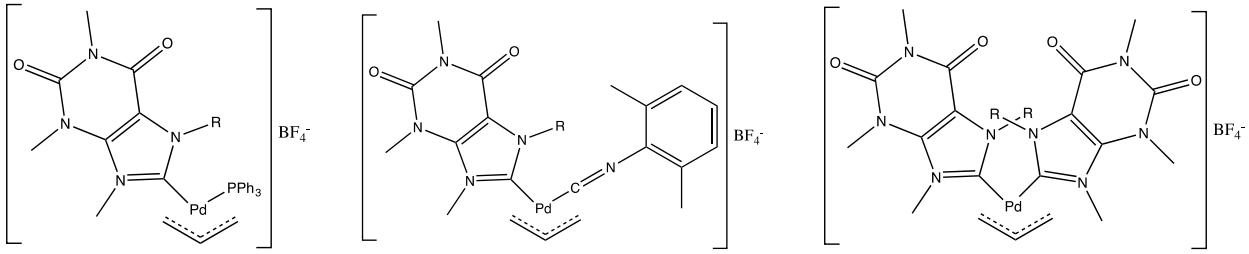

Fig.1 Chemical structures of the theophylline-based Pd(II) allyl complexes (R= Me, Bn, Phpropargyl)

The palladium complexes reported above, characterized by spectroscopic techniques (i.e. IR and NMR), exhibit a good antiproliferative activity against A2780 and SKOV-3 human cancer cell lines.

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