2.4.6 Research Area "α-Cationic Phosphines" (M. Alcarazo)

Involved: H. Tinnermann, E. González, J. Dube, S. Holle, E. Haldón, L. Gu, P. Linowski, A. Zannardi, L. Nicholls

Objective: Synthesis of structurally differentiated α-cationic phosphines/arsines and evaluation of their potential as ancillary ligands in catalysis.

Introduction: The world of ligands is dominated by anionic and neutral species. This is not surprising considering that they have been designed to coordinate metals, which usually behave as Lewis acids. Cationic ligands are exceptions and when they are used, the positive charged group is mostly located at a remote position from the donating atom. However, beneficial effects can be expected from the incorporation of positive charges in close proximity to the donor position. The strong –I inductive effect of positive charges reduces the σ-donor abilities of α-cationic phosphines. Simultaneously, the new very low lying σ*(P-C^+) orbitals increase their π-acceptor character and, as a consequence, the global electron donation of these ligands to the metal is quite low.

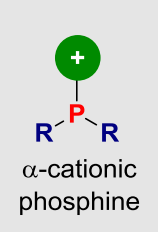
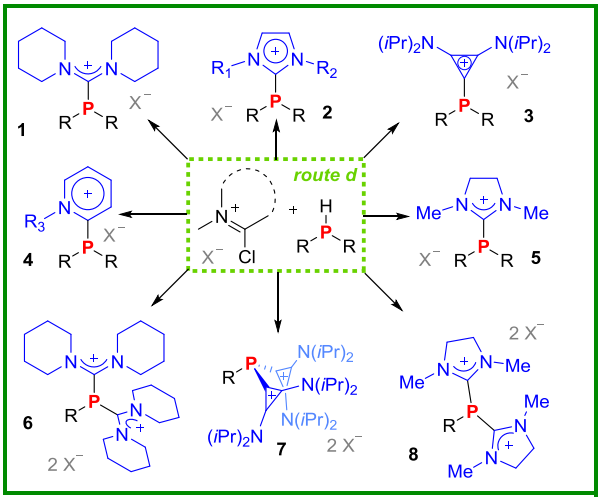


Fig. 1

This may have interesting consequences in catalysis: if the rate-determining step of a catalytic cycle is facilitated by an increase of the Lewis acidity at the metal center, an acceleration of the process is expected by the use of such ancillary ligands. Interestingly, this situation is found more frequently than one might think: many common elementary steps involved in catalytic cycles, such as reductive eliminations, coordination of substrates to metals, or the attack of nucleophiles to coordinated substrates, belong to this category and are often fostered by electron poor metal centers.

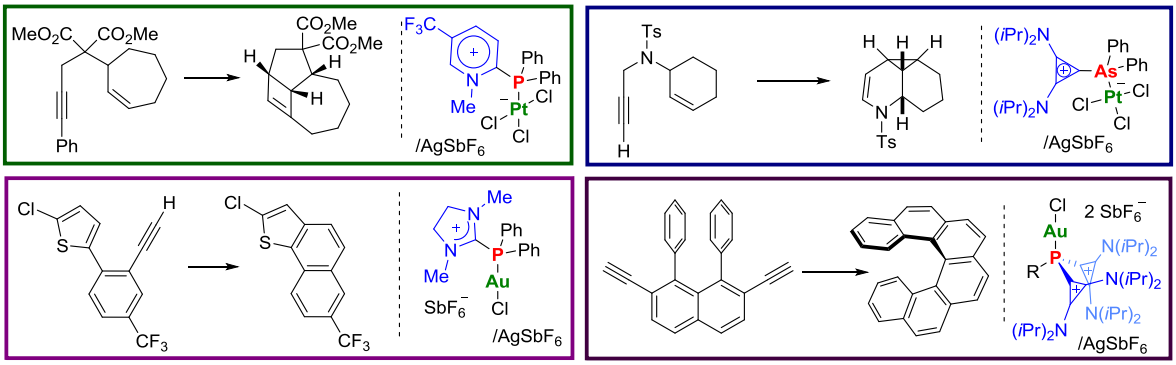
Results: We have implemented a general synthetic method for the synthesis of α-cationic phosphines based on the reaction of secondary phosphines and Vilsmeier-type salts. The availability of both starting materials and the high yields of the condensation reactions make this route very reliable even on multigram scale.
Since then, the repertoire of α-cationic phosphines incorporated to the ligand tool box has been truly expanded, and it now includes cyclopropenio-, imidazolinio-, pyridinio-, and formamidiniophosphines, **1**-**8** respectively (Scheme 1). Moreover, α-dicationic phosphines and α-cationic arsines can be prepared after only small variations of this synthetic methodology.



Scheme 1. Synthetic route for the preparation of mono- and dicationic phosphines.

The structural analysis of compounds **1-5** reveals two parameters that are crucial in understanding their coordination properties. The central phosphorus atom of **1-5** displays a pyramidal environment (sum of angles around P1: 300-318°, depending on the steric demand of the substituents), while all P-C(+) bonds lengths are, within experimental error, very similar to those of the other two P-C(Ph) bonds. These observations suggest that the non-shared electron pair is retained at phosphorus. For this reason the coordination chemistry of cations **1-5** seems to be as rich as that of traditional phosphines; up to now the formation of complexes with Au, Ag, Cu, Pt, Pd, Ni, Ir and Rh have been described. On the other hand, dicationic phosphines are less prone to coordinate metals. Up to now, we have only been successful on the preparation of Pt(II), and Au(I) derivatives of **7**.

Illustrative examples of the use of the newly prepared cationic phosphines in π-acid catalysis are depicted in Scheme 2. In these cyclisation processes the rate determining step is usually the attack of the nucleophile to the activated alkyne; therefore, the employment of cationic ligands that augment the Lewis acidity at the metal center proves beneficial. The reaction rates observed with cationic ancillary phosphines are between 20 and 500 times faster than those measured when Ph_3P-derived catalysts are used under otherwise identical conditions.



Scheme 2. Selected examples of the use of α-cationic phosphines in π-acid catalysis.

Future directions: We anticipate that the intensive acceleration effects observed in π-acid catalysis by the use of α-cationic phosphines might have tremendous implications in the area of asymmetric catalysis, where catalysts able to work at lower temperatures are usually required to obtain good enantiomeric excess. The development of chiral versions of the ligands prepared is one of our current research topics.

Publications resulting from this research area: 49, 51, 53-55, 57, 59, 60

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Cooperations: W. Thiel (Mülheim/Ruhr, DE)

2.4.7 Research Area "Development of New Electrophilic Transfer Reagents" (M. Alcarazo)

Involved: G. Talavera, J. Pena, B. Waldecker, A. Barrado, Y. Zhang, A. Zielinski

Introduction: The unique ability of hypervalent iodine compounds to act as electrophilic group-transfer reagents has been extensively exploited during the last several years in a variety of synthetically useful transformations. These include trifluoromethylation, alkynylation, arylation, amination, halogenation and cyanation of a wide variety of electron-rich substrates under mild conditions. Considering this tremendous synthetic utility, it is surprising that other structurally related scaffolds, yet not based in iodine, have not been evaluated for similar purposes. We recently envisaged that imidazolium sulfuranes **A,** that are isolobal to I(III) species **B** and exhibit the key three-center four-electron bond motif, might be considered alternative platforms for the development of new electrophilic group-transfer reagents (Figure 1).

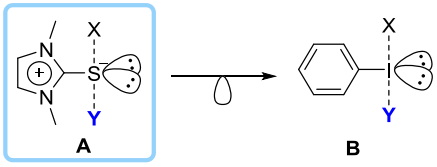
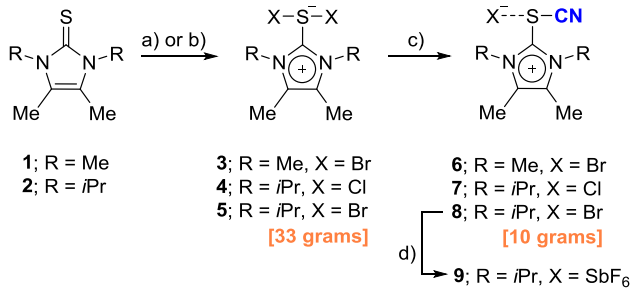


Fig. 1. Isolobal relationship between I(III) species and sulfuranes.

Objective: The implementation of this working hypothesis to the specific design of new sulfur-based electrophilic transfer reagents. Specifically, we have already developed cyanation, alkynylation and thioalkynylation reagents.

Results: We submitted thioureas **1** and **2** to previously described halogenation conditions, and obtained the corresponding hypervalent sulfur compounds **3-5** as bright yellow to orange solids in high yields and analytic purity (Scheme 1). Subsequent addition of one equivalent of Me_3SiCN caused the immediate disappearance of the color and formation of the desired imidazolium thiocyanates **6-8**. Compounds **6-8** were isolated as air stable pale yellow solids in excellent yields, and can be stored at room temperature for months without evident decomposition. Interestingly, compounds **6-9** depicted excellent ability to transfer



Scheme 1. Synthesis of 2-thiocyanoimidazolium salts.

the CN group to organic nucleophiles such as amines, sulfides, enolates, enamines, activated methylenes and electron rich aromatic compounds (Figure 2).

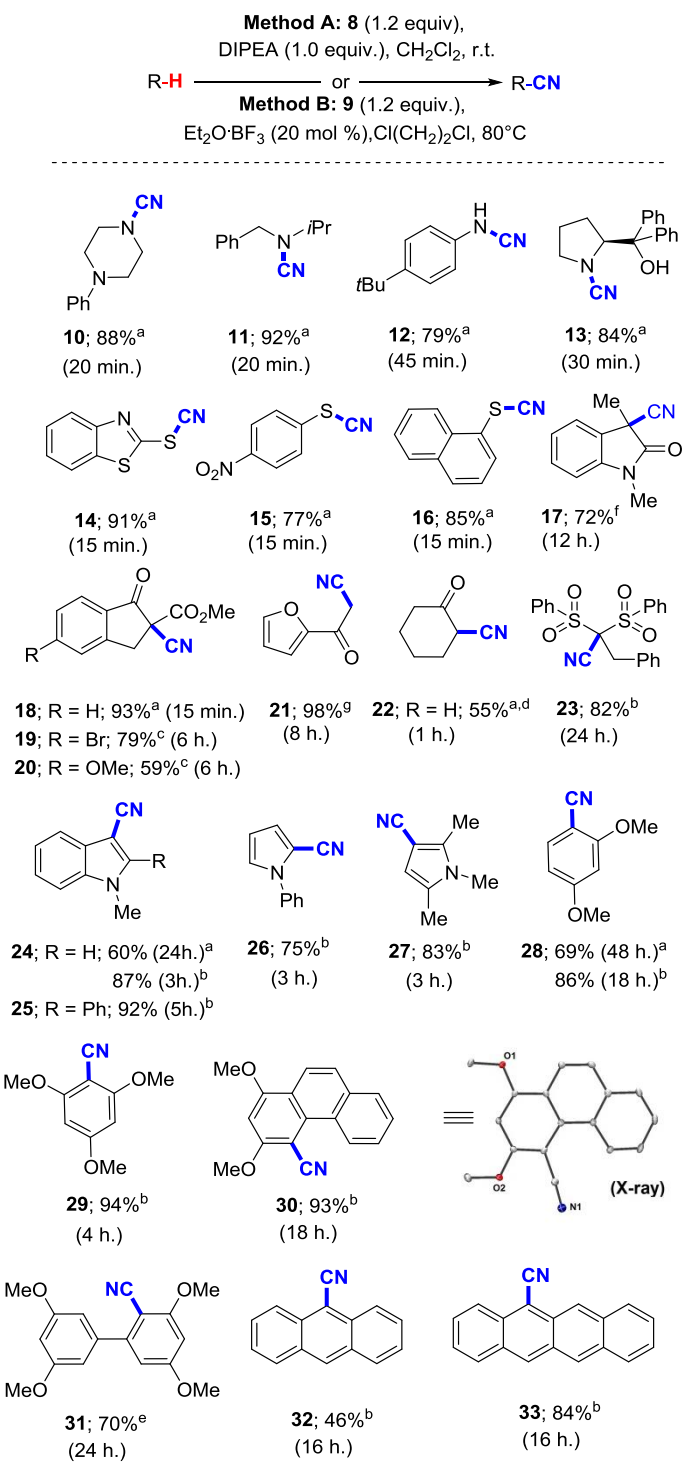
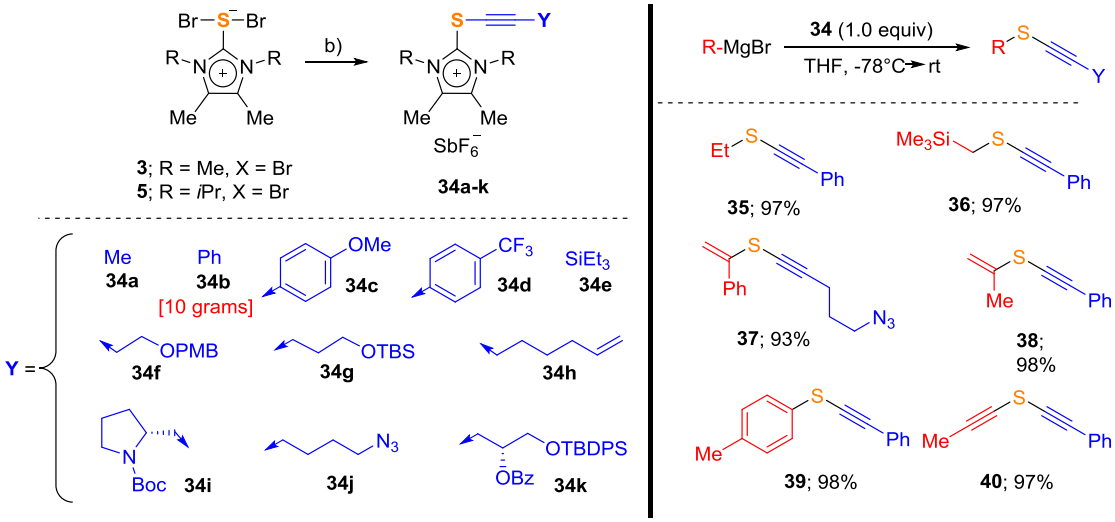


Fig. 2. Substrate scope of the electrophilic cyanation using 2-thiocyanoimidazolium salts **6-9**.

Encouraged by this discovery we set up to explore whether alkynylthioimidazolium salts **34a-k** could also participate in this transformation. Thus, a series of these compounds bearing different functionalizations on the alkyne rests was prepared by reaction of **5** with the desired alkynylzinc bromide. However, already during preliminary investigations, we came across an unexpected finding: simple commercially available Grignards regioselectively attack these salts *at the sulfur atom* affording the corresponding alkynylthioethers in excellent yields (Scheme 2). This unique behavior makes alkynylthioimidazolium salts convenient synthetic equivalents of a formal $[R-C\equiv C-S]^+$ cation.

Alkyl-, aryl-, alkenyl- and even alkynyl-Grignard reagents were found to smoothly react under optimized conditions with salts **34a-k**, providing a library of alkynylsulfides **35-40** in good to excellent yields. Specifically, the robustness and applicability of this transformation is highlighted by the successful preparation of

fairly hindered thioethers, vinylthioacetylenes, and a series of asymmetric bis(alkynyl)thioacetylenes that are non-obvious to obtain through other routes. Note however, that the preparative significance of this method is limited at this stage by the use of Grignard reagents.



Scheme 2. Synthesis and reactivity of 2-alkynylthioimidazolium salts.

Future directions: The potential of imidazolium sulfuranes to become platforms for the development of new reagents able to promote the umpolung of synthetically useful organic groups has been demonstrated. Ongoing studies in our laboratory intend to demonstrate the generality of the concept, and to further evaluate the synthetic utility of the new reagents.

Publications resulting from this research area: 58

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