

Muñiz Research Group



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Abstract

The Muñiz group has continued the development of new synthetic methodology for advanced oxidative amination of organic molecules. For 2013, work in the area included the development of new reactivity within the

palladium(II/IV) catalysis manifold as well as in the field of hypervalent iodine(III) reagents. With respect to the latter, the group has succeeded in the preparation and structural characterization of entirely new reagents of the type $\text{ArI}[(\text{NSO}_2\text{R})_2]_2$. These compounds provide unprecedented reactivity in a series of C-N instalment events.

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We have continued working on the two major research themes from recent years, which confer to the development of new homogeneous amination chemistry based on the methodology of high oxidation state reagents and catalysts. To this end, we focus on palladium(II/IV) catalysis and iodine(III) reagents. Again, both of these projects have demonstrated to provide significant synthetic possibilities.

Palladium catalysis

We were invited by the editors to provide a general overview on the synthetic potential of our transition metal catalyses for the intramolecular diamination of alkenes. This review also includes some additional, previously unpublished results that were thereby made available to the synthetic community. We have then continued our proposed work on the development of new palladium oxidation catalyses. Our previous development of the first general palladium catalysed vicinal diamination reaction of internal alkenes led us to seek a collaboration with the groups of Professor Stahl in Wisconsin, USA and Professor Liu in Shanghai, China, to work on the related aminoacetoxylation reaction. Based on X-ray analysis, deuterium labelling and kinetic experiments, we arrived at an advanced mechanistic understanding of the underlying palladium(II/IV) catalysis of this process. Furthermore, we provided an optimised protocol for the aminoacetoxylation of internal and terminal alkenes, which proceeds with entire regio-, diastereo- and chemocontrol. It is of significant synthetic importance that the new protocol provides conditions that render the initial reaction more applicable as the alkene substrate can now be used as the limiting compound in this transformation.

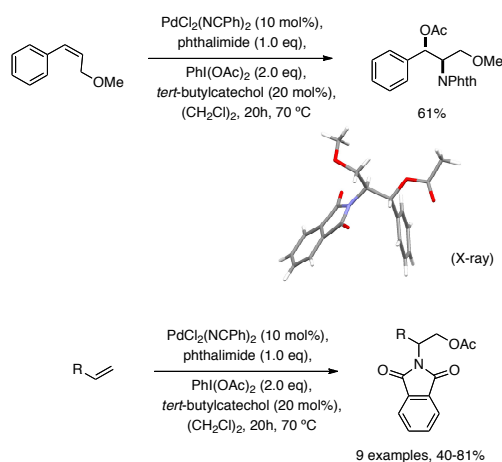
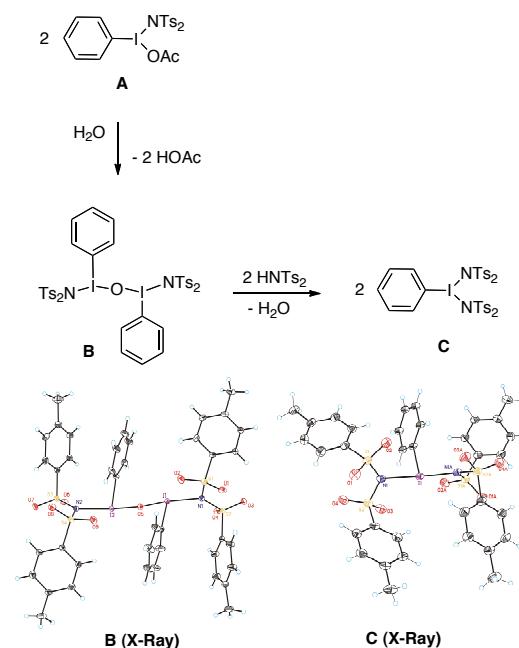


Fig. 1 - Stereochemical assignment of the aminoacetoxylation product from palladium-catalysed oxidation of an internal alkene and general reaction conditions for this transformation.

To demonstrate this context, we provided a significantly enhanced substrate scope of the aminoacetoxylation reaction of terminal alkenes with respect to functional group tolerance (9 representative examples, 40-81% yield).

Metal-free amination by hypervalent iodine chemistry

We have succeeded in the isolation and full structural characterisation of the hypervalent iodine reagents that promoted seminal new intermolecular amination reactions as previously developed by us. These specific results were included in our report for the year 2012. The identification of the actual active reagents has now set the molecular basis to rationalise this new reactivity.⁵ To accomplish the synthesis of new hypervalent iodines with inherently new reactivity, we started from the previously described compound **A**, which displays a unique iodine-nitrogen single bond. Upon exposure of **A** to moisture, this compound converts into the new dimeric compound **B**, in which two iodine(III) groups are bridged through a μ -oxo bond. Protonolysis of the latter furnishes the new iodine(III) compound $\text{PhI}(\text{NTs}_2)_2$ **C**, which contains two defined iodine-nitrogen single bonds (Figure 2).



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Fig. 2 - Synthesis of new hypervalent iodine(III) reagents with defined iodine-nitrogen single bond.

It is of utmost importance that the new compounds **B** and **C** contain iodine-nitrogen bonds, which upon solution dissociation lead to electrophilic iodine and nucleophilic nitrogen. Such behaviour is unprecedented for iodine(III) reagents and thus significantly broadens the synthetic application of such reagents. This reagent $\text{PhI}(\text{NTs}_2)_2$ **C** has enabled unprecedented reactivity in the past and it can be expected that it will equally provide significantly new reactivity within future exploration. To underline this expectation, the following Figure 3 displays some remarkable examples on new intermolecular amination, where the reagent $\text{PhI}(\text{NTs}_2)_2$ overrides existing nucleophilic groups within the organic substrate.

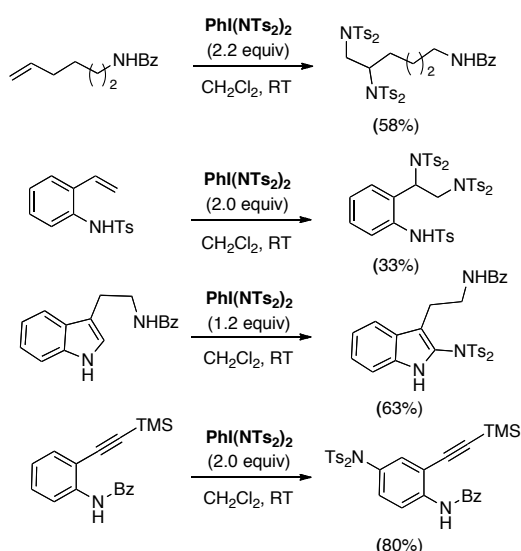


Fig. 3 – Selective intermolecular amination reactions overriding potential intramolecular reactivity.

Finally, the isolation of compound **C** and its unprecedented synthetic reactivity have led us to explore the accessibility of binuclear iodine(III) derivatives displaying defined iodine-nitrogen single bonds. Such an enterprise was indeed found possible and the following synthetic transformation of 2,2'-diiodo biphenyl into a derivative with two discrete $\text{I}(\text{NTs}_2)_2$ groups was accomplished (Figure 4).

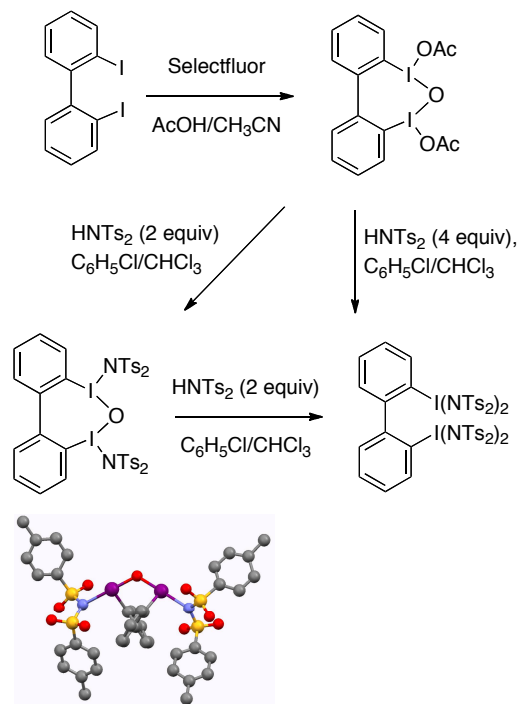


Fig. 4 – Synthesis of new biaryl reagents with discrete $\text{I} - \text{NTs}_2$ bonds

This successful sequential transformation led to an exploration of related biaryl backbones such as the bisnaphthalene moiety. For this type of reagents, we investigated the enantioselective diamination of alkenes as a standard reaction (Figure 5).

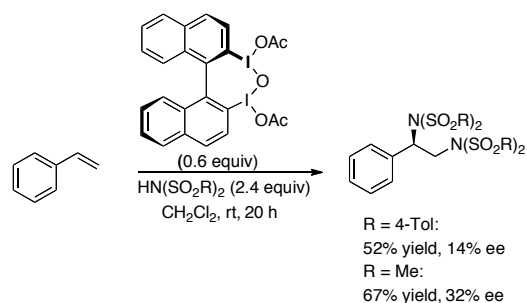


Fig. 5 – Enantioselective diamination of styrene based on a binaphthyl reagent

While the obtained enantioselectivities are less impressive than the ones obtained with a former protocol from our group, the biaryl backbone can apparently exercise enantiocontrol in this type of reactions. We are currently exploring sterically more elaborate derivatives with a 3,3'-substitution pattern that should allow enhancing enantiomeric induction.

Articles

“A New *Remote Control* for Traceless meta-C-H Olefination of Phenols”

ChemCatChem. **2013**, *5*, 3502

C. Martínez, K. Muñiz

“Palladium Catalyzed Intermolecular Aminoacetoxylation of Alkenes and the Influence of PhI(OAc)₂ on Aminopalladation Stereochemistry”

J. Org. Chem. **2013**, *78*, 6309

C. Martínez, Y. Wu, A. B. Weinstein, S. S. Stahl, G. Liu, K. Muñiz

“Metal-free Catalytic Vicinal Diamination of Alkenes”

Pure & Appl. Chem. **2013**, *85*, 755

K. Muñiz

“Oxidative Diamination Promoted by Dinuclear Iodine(III) Reagents”

Org. Lett. **2013**, *15*, 1008

C. Röben, J. A. Souto, E. C. Escudero-Adán, K. Muñiz

“Defined Hypervalent Iodine(III) Reagents incorporating transferable Nitrogen Groups: Nucleophilic Amination through Electrophilic Activation”

Angew. Chem. Int. Ed. **2013**, *52*, 1324

J. A. Souto, C. Martínez, I. Velilla, K. Muñiz

“Development of Intramolecular Vicinal Diamination of Alkenes: From Palladium to Bromine Catalysis”

J. Org. Chem. **2013**, *78*, 2168

C. Martínez, K. Muñiz