# Muñiz Research Group



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## Abstract

The Muñiz group devotes efforts to develop sustainable synthetic methodology for advanced oxidative transformation of organic molecules. For 2017, work in this area has provided new transformations that are based on molecular iodine reagents and catalysts. Prominent examples include pioneering work on enantioselective alkene diamination reactions under intermolecular reaction control and radical-based C-H amination reactions.

We have accomplished significant new transformations in the area of homogeneous catalytic amination reactions. To this end, we have identified versatile molecular iodine catalysts that allow to carry out alkene difunctionalisation in an ionic, and C-H oxidation in a radical manner.

**Iodine(I/III)-catalysed diamination of styrenes**

We continuously expand our expertise on chiral hypervalent iodine chemistry. After the development of an iodine(I/III)-catalysed dioxygenation, we have now succeeded in the identification of a suitable chiral iodine iodine(I) compound **A** as catalyst for the development of the corresponding enantioselective catalytic diamination of styrenes (Fig. 1).
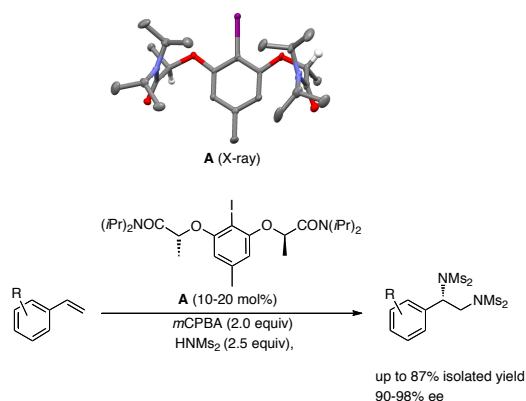


**A** (X-ray)



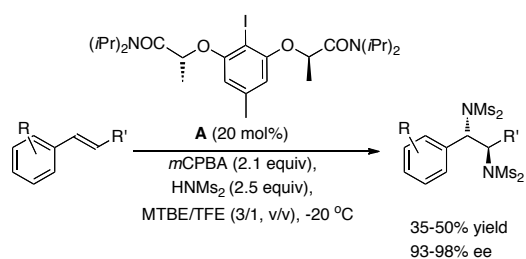Fig. 1 – Catalytic enantioselective diamination of styrenes: reaction.



Fig. 2 – Catalytic enantioselective diamination of internal styrenes.

The reaction is not limited to terminal styrenes, but can also be applied to the substrate class of internal alkenes. In these cases, the reaction proceeds with complete diastereoselectivity and with exceedingly high enantioselectivity (Fig. 2). The obtained outcome outperforms our earlier stoichiometric transformation developed in 2011. The mechanism of this reaction is based on an iodine(I/III) manifold, which initiates with the

oxidation of catalyst **A** in the presence of *m*CPBA as oxidant and bismesylimide as nitrogen source (Fig. 3). The potential background reaction by *m*CPBA could be suppressed by choice of an appropriate solvent mixture and comparably low reaction temperature. In this manner, **A** provides the corresponding diimido iodine(III) catalyst, which represents the only competent oxidant for alkene difunctionalisation. Dissociation of one imido group from iodine(III) leads to formation of a cationic iodine(III), which engages in an effective differentiation of the enantiotopic alkene faces of the styrene substrates. Regioselective amination of the coordinated styrene at the benzylic position proceeds with excellent diastereoselectivity, and the resulting amino-iodinated intermediate undergoes intramolecular nucleophilic addition of one sulfonyl group to the neighbouring C-I bond, thus leading to reductive elimination of the initial catalyst **A**. The resulting cyclic intermediate follows a Prevost mechanism, in which nucleophilic addition of the remaining bissulfonimide proceeds at the homobenzylic position, thus furnishing the final diamine products with full diastereo- and high enantiocontrol.
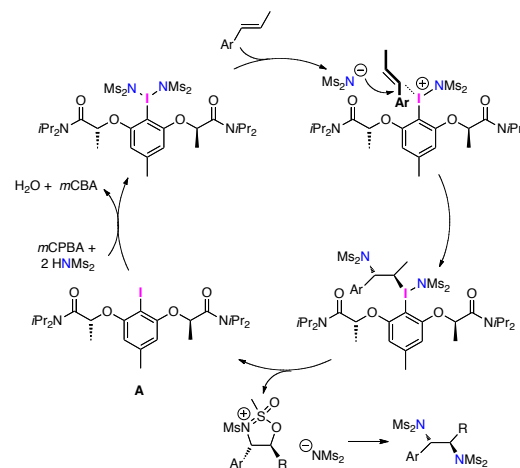


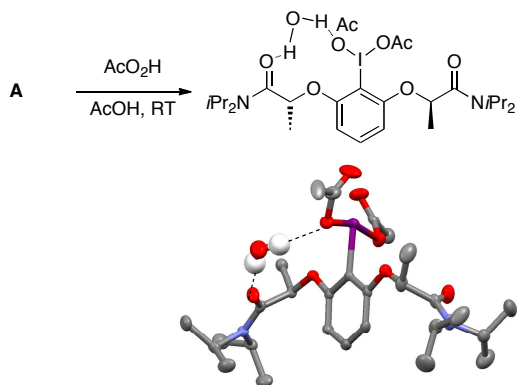Fig. 3 – Catalytic enantioselective diamination of styrenes: catalytic cycle.

Fig. 4 – Catalytic enantioselective diamination of styrenes: catalyst.

Although the active iodine(III) catalyst state has not be determined so far, the corresponding diacetoxyiodine(III) derivative was isolated and structurally characterized including X-ray analysis (Fig. 4). It suggests that the supramolecular stereochemical environment may comprise effective intermolecular hydrogen bonding between protic molecules, the amide group of the catalyst side chain and the heteroatomic groups at iodine(III).

This observation should be instructive for the development of future enatioselective iodine(I/III) catalysis.

### Iodine-catalysed deraomatisation

Making use of our earlier chiral iodine catalysts for enantioselective oxidation, the group has explored its application in the intermolecular dearomatization of phenols using water as nucelophile (Fig. 5). This successful reaction has broadened the scope of our chiral catalysis with lactate-derived iodine compounds. Ongoing work is directed to the improvement of the enantioselectivity of the reaction.
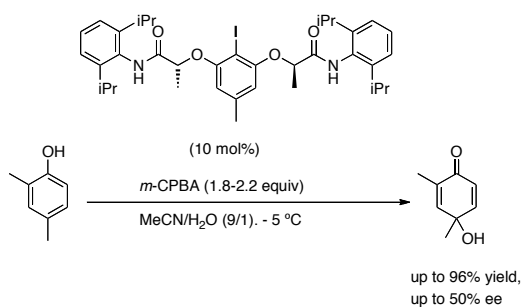


Fig. 5 – Enantioselective dearomatisation under iodine(I/III) catalysis.

Finally, a new aryliodine bearing a pyridinyl substituent was developed. This compound effectively catalyses the diacetoxylation of alkenes with peracetic acid as terminal oxidant (Fig. 6). The oxidation product from aryliodine oxidation is the corresponding pyridine-coordinated iodosobenzene, while the active catalyst is formed upon addition of acetic acid. Both iodine(III) structures were isolated and determined by X-ray analysis.
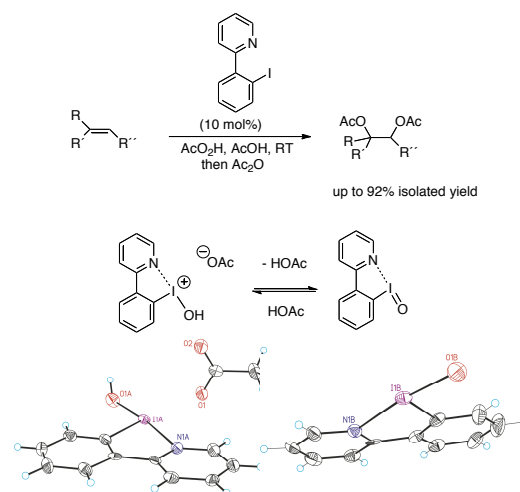


Fig. 6 – Reductive C-N bond formation from diaryliodonium compounds: synthesis of sterically congested anilines.

### Iodine-catalysed C-H amination

Our occupation with the development of iodine catalysts for a catalytic Hofmann-Löffler reaction has been a major theme in the group. Following earlier work, we have isolated a number of stabilized iodine(I) compounds (Fig. 7), which constitute active catalysts or catalyst precursors for the iodine(I/III)-catalysed intramolecular C-H amination. These compounds could also be employed as reagents in the vicinal difunctionalisation of alkenes.
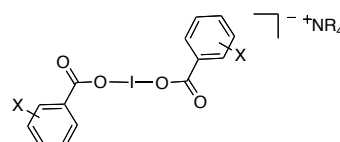


Fig. 7 – Isolated iodine(I) derivatives.

The development of new catalysis concepts for the intramolecular C-H amination was continued investigating conditions of photoredox catalysis as the terminal oxidation system. Using organic

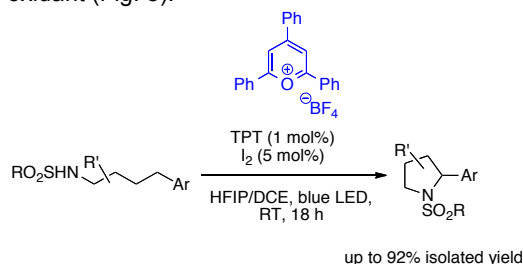dye TPT an efficient process could be developed, which requires only air as terminal oxidant (Fig. 8).



Fig. 8 – Development of an iodine(-I/I) catalysis for intramolecular C-H amination.

This reaction opens new possibilities regarding catalyses, which include multiple steps of photochemistry. For the present case, both the final reoxidation of iodine as well as the initiation of the radical process are induced by light. Their compatibility was deduced from combined synthetic and computational experimentation. The latter, carried out in collaboration with Prof. Reiher at the ETH Zurich, clarified that the crucial N-I bond activation is a direct process, which proceeds over a large wavelength range. Fig. 9 displays the corresponding LUMO of the N-iodinated intermediate.
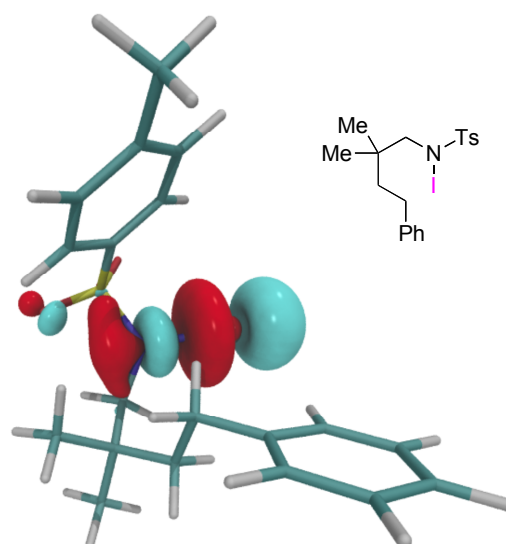


Fig. 9 – N–I anti-bonding LUMO of the N-I catalyst state in a closed conformation.

## Articles

"Cooperative Light-Activated Iodine and Photoredox Catalysis for the Amination of Csp3-H Bonds "
*Angew. Chem.* **2017**, *129*, 8117-8121
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P. Becker, T. Duhamel, J. C. Stein, M. Reiher, K. Muñiz

"Catalytic Asymmetric Diamination of Styrenes "
*J. Am. Chem. Soc.* **2017**, *139*, 4354-4357
K. Muñiz, L. Barreiro, R. M. Romero, C. Martínez

"Selective Piperidine Synthesis Exploiting Iodine-Catalyzed Csp3-H Amination under Visible Light "
*ACS Catal.* **2017**, *7*, 4122-4125
H. Zhang, K. Muñiz

"Enantioselective 4-Hydroxylation of Phenols under Chiral Organoiodine(I/III) Catalysis "
Synthesis **2017**, *49*, 2901-2906
K. Muñiz, L. Fra

"Vicinal Difunctionalization of Alkenes under Iodine(III) Catalysis involving Lewis Base Adducts "
*Adv. Synth. Catal.* **2017**, *359*, 1290-1294
K. Aertker, R. J. Rama, J. Oppalach, K. Muñiz

"Dioxoiodane Compounds as Versatile Sources "
*Chem. Eur. J.* **2017**, *23*, 1539
K. Muñiz, B. García, C. Martínez, A. Picinelli