Despite the tremendous progress in organic chemistry in the last half century, the syntheses of most complex molecules still involve an elevated number of steps, generate a large amount of waste, and require time and cost-consuming purification steps. In this context, C-H activation processes have emerged as a promising approach towards greener chemistry, due to their atom and energy efficiency, and the reduced waste generation, thus considerably reducing synthetic costs. In particular, C-H arylation transformations will play an important role in the future, by replacing the highly used –but wasteful– traditional cross-couplings (Suzuki, Negishi, Stille) with cheaper alternatives.

The ultimate application of C-H activation to the synthesis of biaryl compounds is a reaction in which two non-prefunctionalised arenes are cross-coupled. However, several drawbacks remain to be addressed before these methodologies can be widely applied. Firstly, harsh reaction conditions are commonly needed, with temperatures typically exceeding 110°C and/or strong acids required as solvents. Secondly, poor regioselectivities are generally obtained with substituted arenes. Finally, in most oxidative couplings, both coupling partners are activated by Pd(II) or Pd(IV) species that have very similar selectivities, which results in the need for using 30–300 equiv of one of the two arenes to ensure that cross- rather than homo-coupling is achieved.

We hypothesised that a transition metal capable of presenting orthogonal C–H activation selectivities depending on its oxidation state would allow a new approach towards the rational design of oxidative cross-coupling methodologies with high selectivities. This year we demonstrated that Au species present this unique redox-controlled selectivity and highlight their potential use for the design of novel oxidative double C–H activation cross-couplings. These Au-mediated transformations proceed at lower temperatures than current Pd systems, and display excellent regioselectivities, high cross- versus homo-coupling selectivities (thus avoiding the need for vast excesses of the arenes), and are compatible with Pd-sensitive groups, such as I and Br.

All the compounds reported in this study have required help from the NMSSC/NMSF for their characterization, in particular for the determination of HRMS to confirm identity of the compounds, and for the determination of isotopic ratios in kinetic isotope effect experiments.

This work has just been accepted for publication in Angewandte Chemie, and is currently in press (doi: 10.1002/anie.201209007)

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