

Gold-catalyzed chemo- and site-selective direct C–H functionalization of phenols with diazo compounds

Phenols motifs are used as common versatile synthons in organic synthesis due to their wide availability and low cost. Thus, C–H functionalization of phenols is highly attractive to the community of synthetic chemistry. In the past decade, many methods have been developed via installing a protective group on the hydroxyl to allow for *ortho/meta/para* functionalization of phenols. One of the most effective methods for direct C–H functionalization is the carbene transfer reaction of diazo compounds catalyzed by transition-metal complexes, such as rhodium, copper, silver, palladium, etc. However, direct C–H functionalization of phenols with diazo compounds remains to be highly challenging because the reactive O–H bond could lead to competitive chemoselective O–H bond insertion in the presence of various transition-metal catalysts.

In a remarkable new strategy recently reported in *J. Am. Chem. Soc.* [1], researchers led by Prof. Lu Liu and Prof. Junliang Zhang at East China Normal University have successfully developed the first example of a gold-catalyzed highly site-selective direct C–H bond functionalization of unprotected phenols and *N*-acylanilines with α -aryl α -diazoacetates and diazoindoles under mild conditions (Figure 1). This method demonstrated chemo- and site-selectivity for the reaction of phenols and diazo compounds, in which the organophosphite-based gold catalyst proved to be the best. This strategy provides a facile synthesis of diarylacetylates, which are important motifs in natural products, bioactive and pharmaceutical molecules, and functional

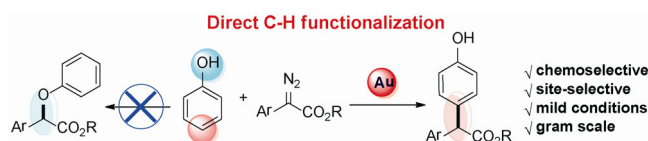


Figure 1 Chemo- and site-selective C–H functionalization of phenols.

materials. This work would broaden the application of gold catalysts in carbene transfer reaction. The salient features of this reaction include readily available starting materials, unprecedented C–H functionalization rather than O–H insertion and cyclopropanation. It should be noted that this transformation is easy to scale-up for gram-scale and requires low catalyst loading (0.5 mol%), giving the products in similar isolated yield. The report by Prof. Zhang *et al.* represents an exciting and promising synthetic tool for natural products and pharmaceuticals, especially in late-stage modification.

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- 1 Yu ZZ, Ma B, Chen MJ, Wu HH, Liu L, Zhang JL. Highly site-selective direct C–H bond functionalization of phenols with α -aryl- α -diazoacetates and diazoindoles via gold catalysis. *J Am Chem Soc*, 2014, 136: 6904–6907