APPLICATIONS OF ORGANOMETALLIC CHEMISTRY FOR CARBON ISOTOPE LABELING

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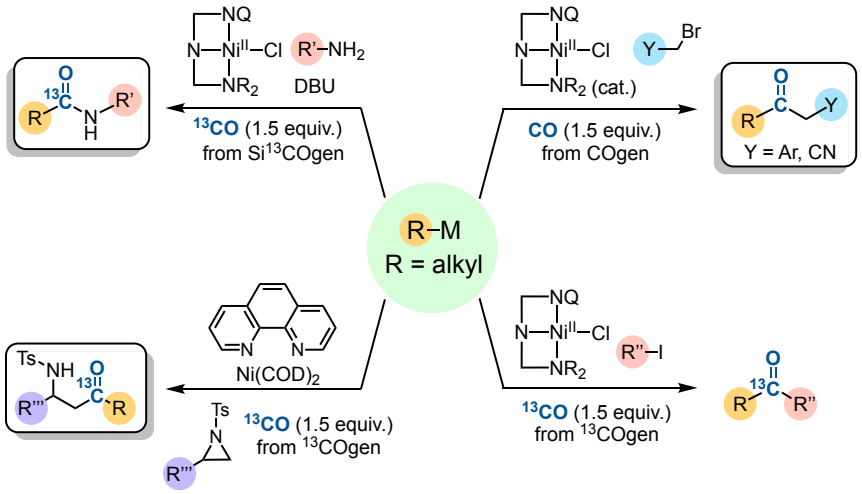
Documented distribution, metabolism, and toxicity investigations of new drug candidates administered to humans represent one of many mandatory requirements by regulative administrations for drug approval. The specific isotope labeling of these candidates with carbon-11, -13 and -14 provides access to useful tagged compounds for undertaking such studies by different means depending on the isotope applied. The development of new synthetic methodologies adaptable to carbon isotope labeling can aid this important hurdle in drug discovery programs by providing rapid access to isotopically labeled pharmaceutically compounds.

Carbon monoxide (CO) represents an important C1 building block for the construction of some of the most fundamental chemical functionalities carrying a carbon-oxygen single or double bond. Transition metal catalysis plays a key role for promoting such transformations. We have earlier shown that the combination of palladium catalysis with CO releasing molecules and the two-chamber reactor COware® provides a convenient and safe means for performing traditional Pd-catalyzed carbonylative couplings, but it is also a platform for the discovery of new carbonylation reactions including an initial CO_2-to-CO reduction step.[1–3] Furthermore, the method can be adapted to ^{13}C- and ^{14}C-isotope labeling,[3] and provides a suitable setting for developing efficient carbonylation reactions with ^{11}CO in combination with organometallic reagents.[4] Herein, I provide a short overview of our latest findings in this area, and also discuss our efforts to develop viable carbon isotope labeling techniques applying Ni-mediated carbonylations with aliphatic substrates.[4]



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