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Cobalt catalyzed multicomponent cyclizations of enynes and alkenes

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Synthesis of complex organic molecules has relied heavily on the use of stoichiometric organometallic reagents. Strategies such as metal-catalyzed cycloisomerization bypass the need for these oftentimes harsh reagents and are valuable for constructing cyclic frameworks from simple unsaturated carbon sources. An important extension of this cyclization methodology is the incorporation of additional components accompanying the initial annulation. Through our studies we learned that cationic cobalt complexes can catalyze an intramolecular enyne cyclization, and subsequently form carbon-carbon bonds through intermolecular incorporation of feedstock alkenes into a presumed metallacycle intermediate. This strategy allows access to complex alicyclic and heterocyclic compounds from an earth abundant metal catalyst and readily available materials. Of note, is the complimentary reactivity and selectivity in this newly discovered cationic cobalt reaction manifold as compared to analogous rhodium and ruthenium catalysis. We discovered that product selectivity is dependent upon alkene identity, with activated alkenes and unactivated alkenes inserting into opposite sides of the cobaltacyclopentene intermediate. This remarkable selectivity provides access to two different motifs accompanying the cycle formed, either a linear diene or a styrene with a pendant functionalized acrylate. Over 25 different medicinally relevant pyrrolidines were accessed in this fashion and further elaborated on by post-synthetic modifications. In addition, the enantioselective variant of this reaction is also explored with selectivities up to 77% ee.