Transition metal-free alkynylation of enaminomaleimides with α-chloronitroolefins- Syntheses of new functionalized maleimides

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Maleimides, or 1H-pyrrole-2,5-diones, represent a key electrophilic heterocyclic motif in organic chemistry. Over the past century, this five-membered heterocyclic imide core has been identified in diverse families of natural products,[1] synthetic pharmaceutical molecules,[2] and functional polymers,[3] offering broad scientific and technological applications. These maleimides are recognized for their C=C double bond conjugated to two carbonyl groups, which confers electrophilic properties enabling Michael addition reactions (particularly with thiols) and Diels–Alder cycloadditions with dienes. However, their (pro)nucleophilic characteristics remain poorly characterized in the literature and largely unexplored. A method to probe their nucleophilicity is the utilization of enaminomaleimides, or α-aminomaleimides.[4] They are a subclass of maleimide derivatives in which an amino group is introduced at the α-position (or position C3). During our research aimed at exploring the nucleophilic potential of enaminomaleimides, we serendipitously uncovered a particular reactivity of these species with α-chloronitroolefins. Instead of yielding the anticipated maleimide-fused pyrroles,[5] the reaction resulted in an alkynylation at the C4 position of the enaminomaleimides. Notably, in contrast to conventional alkynylation protocols, this approach successfully avoids the use of transition metals. Furthermore, this reaction exhibits a broad substrate scope, proceeding smoothly with a variety of α-chloronitroolefins and enaminomaleimides to afford the corresponding products in excellent yields (up to 93%). Conducted under mild and operationally simple conditions, this unique reactivity opens a novel synthetic pathway in enaminomaleimide chemistry and offers extensive possibilities for further functionalization.

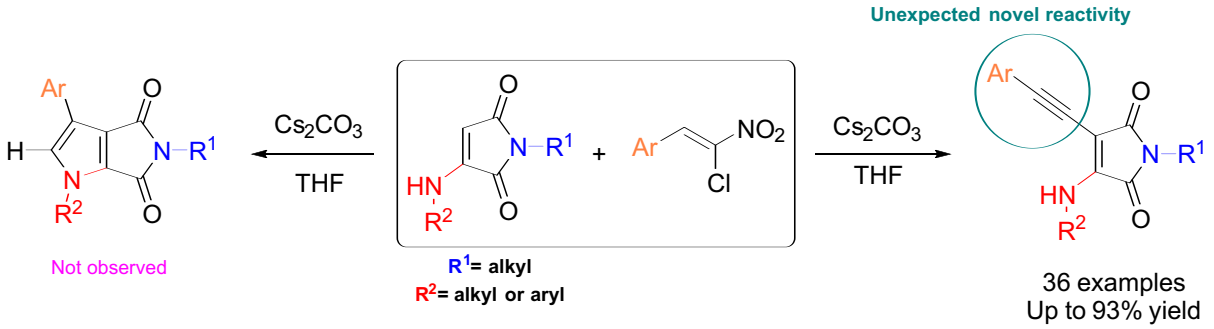

Figure 1: Unprecedented reactivity of enaminomaleimides with α-chloronitroolefins under basic conditions

References

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