Novel reactivity of 2-(Diazobenzyl)chromones in N-H insertion reactions

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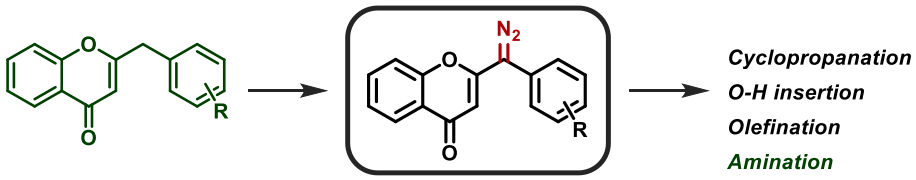
The search for new derivatives of known pharmacophores is never-ending, as new methodologies allow for regioselective functionalization and overall increased drug complexity. Nevertheless, linear synthetic routes are still the most common approach in drug design, leading to the onerous synthesis of precursors molecules. The introduction of the diazo group can provide a solution to this problem, allowing for broad functionalization from a common reagent, from N-H or O-H insertion to cyclopropanation and other cycloadditions.[1] Though powerful, this strategy is limited by the low stability of these compounds, always requiring an α-keto group for its viable purification and isolation.[2]

In this work we synthesized diazo-containing chromone pharmacophores, 2-(diazobenzyl)chromones, via diazo transfer. These were applied in alcohol, cyclopropane and azine synthesis, as well as in the N-H insertion reactions here described in more detail. The unique character of the diazo's conjugation to the chromone ring leads to novel reactivity, yielding either amine, imine, phenazine or oxazine derivatives in good yields. The presence of the chromone nucleus, a privileged structure in drug research due to its anti-cancer, anti-microbial, anti-inflammatory, and anti-cholinesterase activities, attests to their promising biological activity.[3]



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