# NORRISH TYPE II-ENABLED C–H FUNCTIONALIZATION AND ANNULATION

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## INTRODUCTION

Photochemistry provides a rich source of reactivity orthogonal to traditional thermally-driven reactions. A prime example is the Norrish Type II reaction, involving the excitation of a ketone, abstraction of a proton from the γ–carbon, and subsequent cyclization or fragmentation. This transformation offers an excellent means for the selective functionalization of γ–carbons of ketones. Recent methods expand the scope of this process, offering opportunities to functionalize γ–carbons, install new rings, or contract existing rings.

## EXCITATION OF OLEFINS

While the classical Norrish Type II reaction involves the excitation of a carbonyl, recent efforts have allowed an analogous reaction to occur through the generation of a diradical from an alkene. Koert and coworkers obtain cyclobutanes from α–naphthyl acrylates using an iridium energy-transfer catalyst (Figure 1A). Notably, for unsymmetrically substituted *ortho*-alkyl groups, the cyclobutane forms diastereoselectively, such that bulky substituents are oriented *syn* to the ester and ethers are in the position of the $R^4$ group *anti* to the ester.[1] Shi and coworkers accomplish a similar transformation, using biaryl allenes and a ruthenium energy transfer catalyst to generate six-membered rings (Figure 1B). An alternate process occurs when performing this reaction with alcoholic solvent, resulting in the formation of acetals.[2] While the necessity of radical-stabilizing groups limits the scope of these transformations, future investigations of catalysts with higher triplet states could broaden the scope.

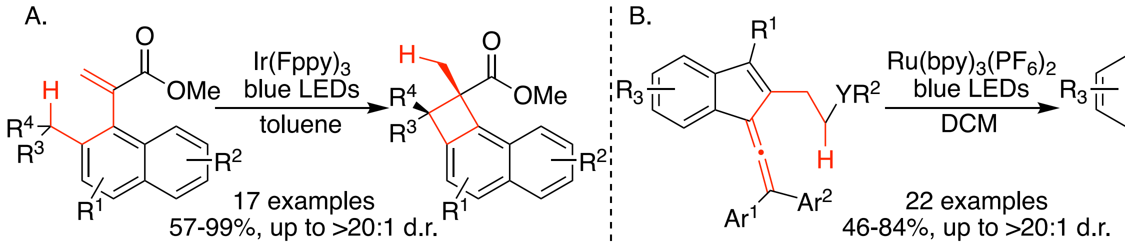

**Figure 1.** Norrish-Yang reactions involving olefins.

## TANDEM ENOL-ELECTROPHILE GENERATION AND REACTION

If a heteroatom is located β to the carbonyl, Norrish Type II fragmentation forms an electrophile in addition to an enol. Subsequently, an aldol reaction occurs between the enol and electrophile. Suárez and coworkers discovered this mode of reactivity when exploring photochemical reactions of α–diketopyranoses (Figure 2A). In these substrates, a cyclopentanol forms from the pyranose, and an intramolecular hemiketalization consumes the photochemically reactive diketone, yielding a stable bicycle.[3] Sarpong and coworkers expanded the scope of this transformation to α–benzoylated heterocycles (Figure 2B). In this case, a hydrogen bond between the ketone and the heteroatom's proton in the product raises the energy required to excite the ketone, allowing the products to be stable under the reaction conditions. Notably, the aldol-type reaction can be performed asymmetrically with the addition of a chiral phosphoric acid catalyst.[4]

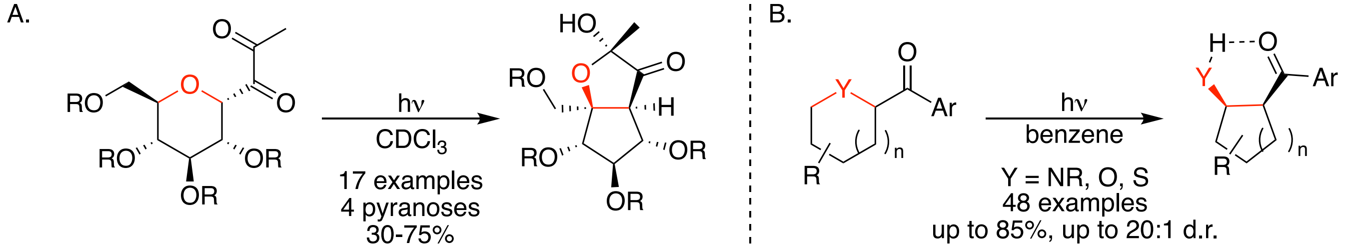

**Figure 2.** Ring formation by Norrish Type II fragmentation followed by aldol-type reaction.

## STRAIN-DRIVEN FUNCTIONALIZATION

The Norrish-Yang reaction affords cyclobutanols or cyclopropyl ketones, in the case of spin-center-shift processes in which the carbonyl radical displaces an adjacent leaving group.[5] The ring strain in these products can be used to drive further reactions. Sarpong and coworkers synthesized α–hydroxy–β–lactams from α–ketoamides of azacycles using a Norrish-Yang reaction and subsequently opened the lactams at either the bond proximal to the azacycle or distal to it. Palladium catalysis with RuPhos achieved the former cleavage, permitting functionalization with aryl, vinyl, and alkynyl groups adjacent to the nitrogen of the azacycle.[6] Alternatively, rhodium with XantPhos led to cleavage of the bond distal to the azacycle, which after decarbonylation afforded a metallated compound that reacted with a Michael acceptor to form an indolizidine.[7] Opatz and coworkers reported a mild organocatalytic opening of cyclopropyl ketones and subsequent radical carbon-carbon coupling to terminal alkynes driven by visible light. While limited in scope, the mild nature of these conditions demonstrated the synthetic utility of the strained products generated by the Norrish-Yang cyclization. Additionally, the Norrish-Yang reaction and formal [3+2] ring formation was also performed in a telescoping fashion.[8]

## REFERENCES

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