

# Tuning Excited-State Pathways for Ultrafast Aza-Quinone Methide Formation

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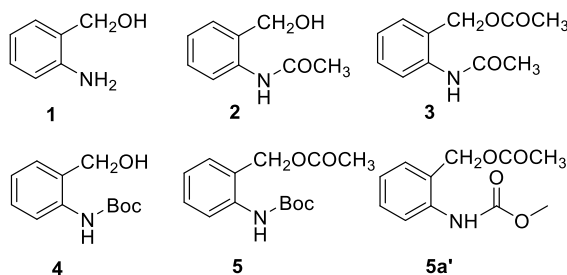
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Aza-quinone methides (aza-QMs) are important intermediates in the synthesis of aza-heterocycles, yet mild and efficient methods for their photochemical generation remain limited. Here, we combine computational and spectroscopic studies to elucidate the excited-state mechanisms governing aza-QM formation from substituted o-hydroxymethylaniline derivatives and to guide the rational design of improved precursors.

Photochemical elimination of H<sub>2</sub>O from 2-aminobenzyl alcohol (**1**) serves as a promising starting point [1]. We show that the reaction proceeds *via* a relatively slow, multistep mechanism involving heterolytic C–O bond cleavage in the S<sub>1</sub> state, formation of a contact ion pair, internal conversion to S<sub>0</sub>, and subsequent deprotonation to yield the aza-QM. In contrast, the newly designed N-Boc-O-Ac-aminobenzyl alcohol (**5**) exhibits a different behavior, where aza-QM formation occurs in an ultrafast, intermediate-free process via the S<sub>1</sub>/S<sub>0</sub> conical intersection.



**Figure 1.** Investigated aniline derivatives **1-5** and **5a'** undergoing photoelimination to aza-QMs

Computational results indicate that C–O bond cleavage in both systems is mediated by higher-lying dissociative  $\sigma^*$  states, which become stabilized upon elongation of the benzylic C–O bond. In **5**, substitution effects further stabilize a low-lying  $n\pi^*$  state and facilitate access to the dissociative pathway, leading to efficient OAc elimination and rapid aza-QM formation.

These mechanistic insights provide a framework for the rational design of aza-QM precursors and highlight how excited-state engineering (systems **1-5**) can be used to control photochemical reactivity in organic synthesis and in biological applications.

## References:

[1] C. Yang, P. Wan, *J. Photochem. Photobiol. A* **80** (1994) 227–232.