New Photo-Induced Alkoxyarylation of 3-Methylene Isoindolinones Using Aryl Diazonium Salts

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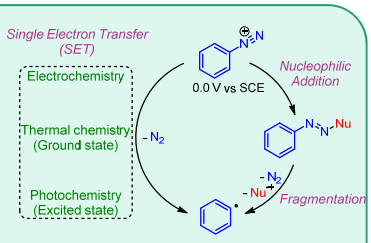
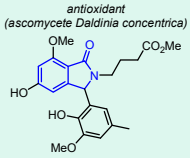
Introduction

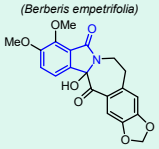
Aryl diazonium salts are a versatile source of aryl radicals. Mechanically, two pathway are available to reduced these species to aryl radical. The first corresponds to a single electron transfer and can be operated via electrochemistry, thermal chemistry or photochemistry. The second one is an addition-fragmentation strategy.[1]



Daldinan A
antioxidant
(ascomycete Daldinia concentrica)

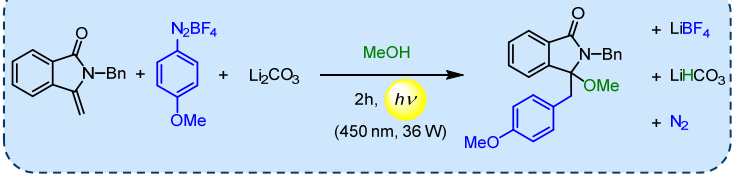


Chilenine
anti-cancer
(Berberis empetrifolia)

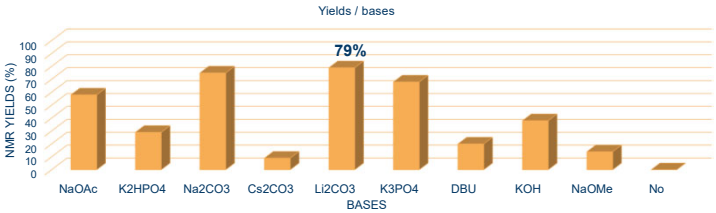


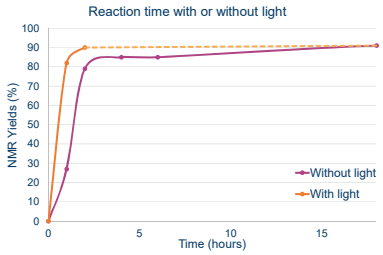
In parallel, **isoindolinones** are widely represented among natural products.[2] Moreover, many of these bio-sourced products have a biological activity. For example, Daldinan A[3] is an antioxidant produced by the mushroom *ascomycete Daldinia concentrica*. A second example is Chilenine,[4] which is used as an anticancer agent and is extracted from *berberis empetrifolia*.

Reaction



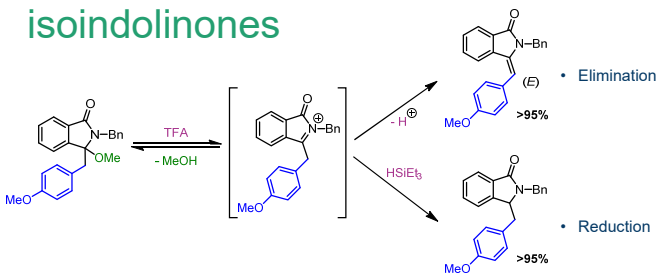
Optimization





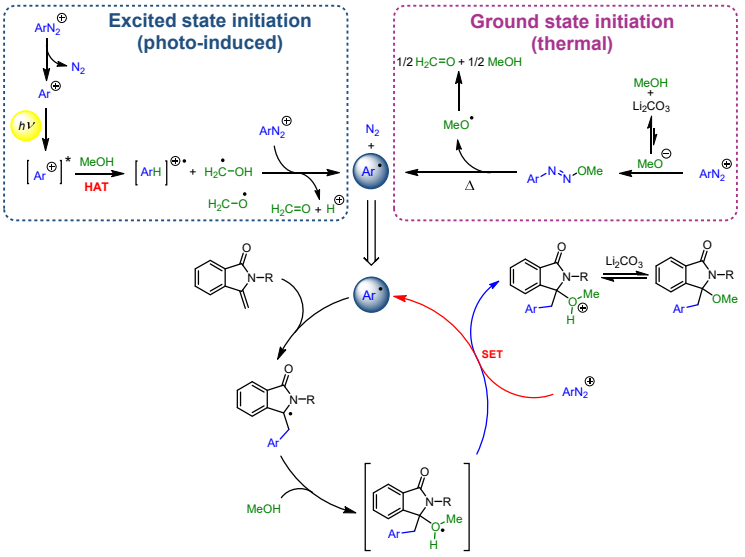
The reaction times were compared with and without irradiation under standard conditions. The reaction peaks at around 90% yield after 16h without irradiation. The same phenomenon is observed under irradiation in only 2h.

Reactivity of 3-methoxy isoindolinones



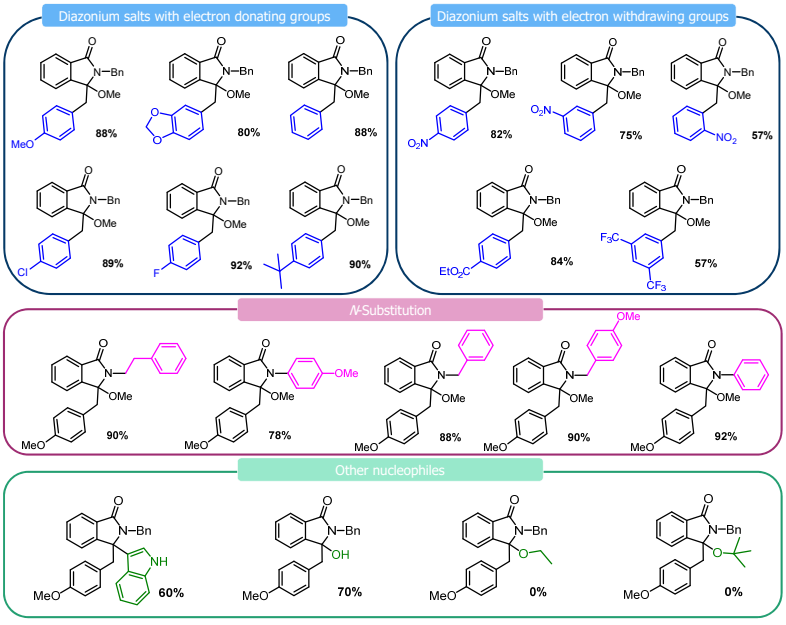
- Elimination
- Reduction

Proposed mechanisms



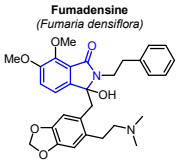
Proposed mechanism[5] of the alkoxyarylation with two complementary initiations steps (excited state[6] and ground state[7])

Scope



Example of a natural isoindolinone that could be obtained via the synthetic route presented in this work.

Fumadensine
(Fumaria densiflora)



References

[1] Tatunashvili, E.; Chan, B.; Nashar, P.E.; McErlean, C.S.P. *Org. Biomol. Chem.* **2020**, *18*, 1812 – 1819.
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UCCS - UMR CNRS 8181
UNIV. LILLE - BATIMENT C3
VILLENEUVE D'ASCQ - FRANCE

Nathan Martin
2nd Year PhD Student
nathan.martin@univ-lille.fr

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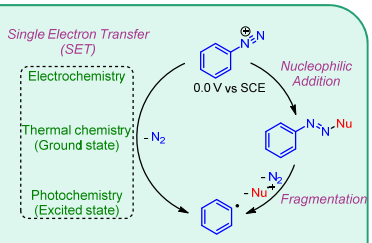

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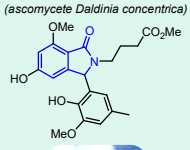

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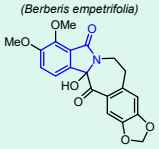

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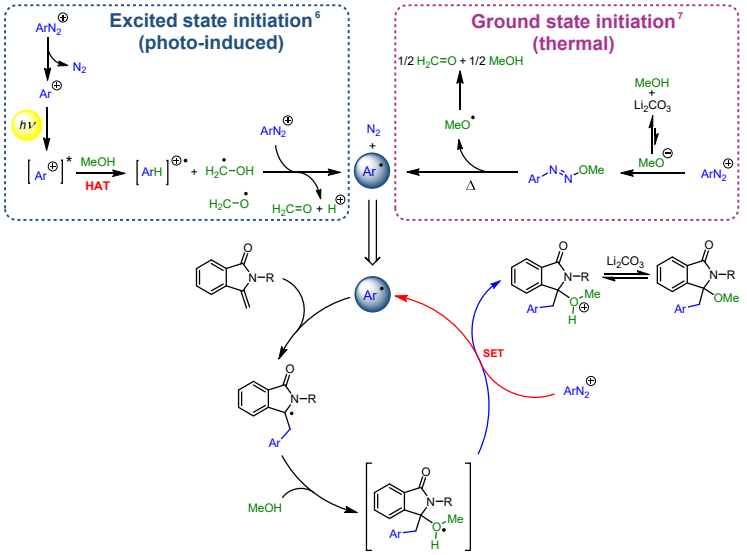

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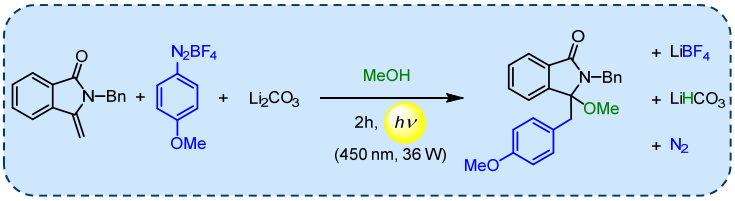

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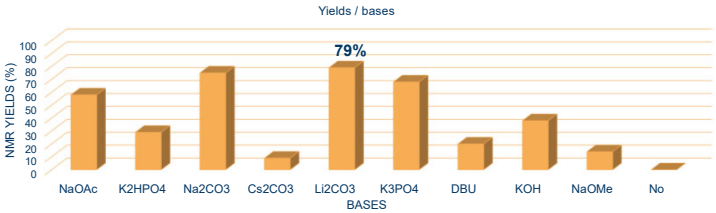

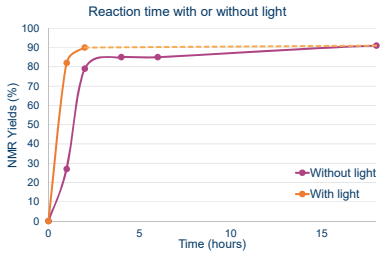

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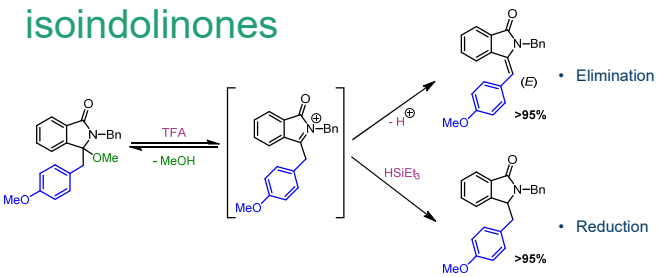

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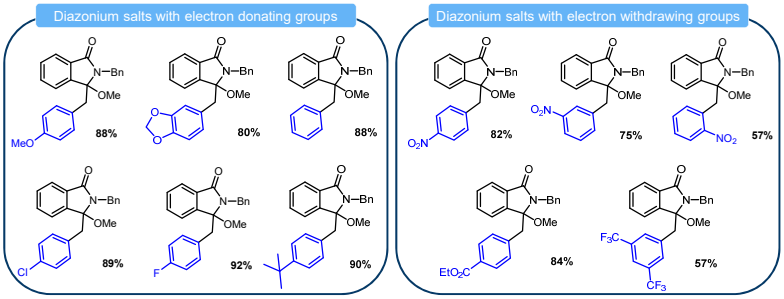

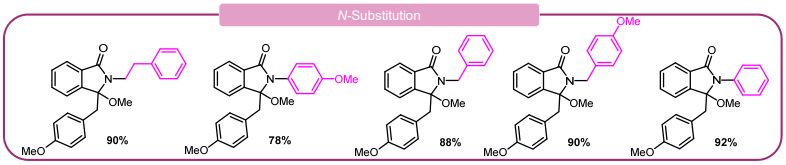

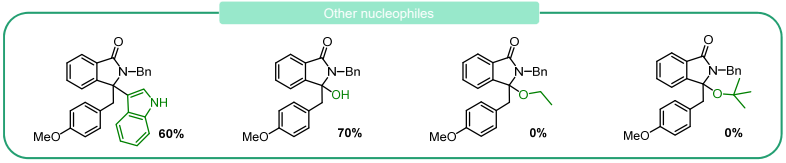

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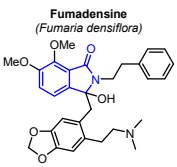

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