Development of Aldehyde-Forming Nef Reaction Initiated by Singlet Oxygen under Mild Conditions

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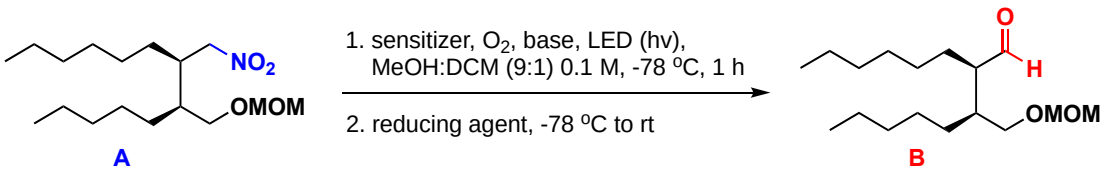
The Nef reaction, a transformation that converts nitro groups (NO_2) into carbonyl compounds such as aldehydes, is a valuable tool in organic synthesis. However, the formation of aldehydes via this reaction is less commonly studied compared to ketones and carboxylic acids, due to the challenges of competing side reactions, such as the Henry reaction. Although some aldehyde-forming reactions have been reported, the scope of applicable molecules is limited due to harsh reaction conditions such as strong oxidants and basic or acidic conditions.[1, 2] This study aims to optimize an aldehyde-forming Nef reaction initiated by singlet oxygen under milder conditions to improve reaction efficiency and yield. Previous work by our group demonstrated the aldehyde formation under visible light irradiation but required 48 hours for satisfactory yields.[3]

The current research focuses on refining these conditions to reduce reaction time and increase yield. Various bases, reducing agents, and sensitizers were evaluated for their effectiveness. Results showed that the combination of Cs_2CO_3 (1.5 eq), Rose Bengal (0.05 eq), and Me_2S (3.0 eq) under visible light at 448 nm provided the best conditions, achieving an 85% yield with complete consumption of the starting material. Other conditions, including different wavelengths, bases, and reducing agents, were also examined, and the optimized conditions demonstrated good functional group tolerance, with aldehydes being formed in moderate to high yields. Additionally, the reduction with $NaBH_4$ instead of Me_2S led to alcohol formation in one pot operation, and the reaction with previous substrates yielded products with higher efficiency than earlier methods. The reaction mechanism was also explained based on ion chromatography analysis. This optimized protocol offers a more efficient and versatile approach to aldehyde synthesis via the Nef reaction.



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