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Distal difunctionalization of aldehydes via the triplet state of Breslow intermediates

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In this issue of Chem Catalysis, Yan and co-workers describe a distal difunctionalization of aldehydes through a triplet state of deprotonated Breslow intermediates, involving an NHC-derived biradical species featuring unique reactivity that is formed upon excitation under thermal conditions resulting from the strikingly low singlettriplet gap.

N-heterocyclic carbene (NHC) organocatalysis has historically been extensively explored through electron-pair transfer processes for a broad range of chemical transformations such as benzoin condensation, Stetter reactions, and acylations (Figure 1Ai).^{1,2} In recent years, considerable interests have emerged in using NHC catalysis to generate radicals as key intermediates via single-electron-transfer (SET) processes for new reactions that are otherwise difficult to realize via ionic processes.³ Whereas the Breslow intermediates (BIs)⁴ display a pivotal role in the electron-pair transformations, the SET reactions rely on two different modes to generate the radical intermediate: one is through oxidation of deprotonated BIs that feature strong reducing capacity in the ground state; the other is through a reduction pathway via acyl azolium intermediate under cooperative NHC and photoredox catalytic conditions (Figure 1Aii).^{5–7}

The nice work by Yan and co-workers in this issue of Chem Catalysis realizes a new strategy for the generation of NHC-bound diradical intermediates by facile thermal excitation of deprotonated mesoionic carbene BIs to their triplet state,⁸ allowing for a variety of distal difunctionalization reactions of aryl aldehydes that include hydro(deutero)defunctionalization, hydrogenation, and reductive alkylation transformations.⁹

The electronic properties of BIs and BI-s derived from a series of NHCs were initially investigated by implementation of density functional theory (DFT) calculations. Intriguingly, a strikingly small singlet-triplet gap as low as 4.0 kcal/mol was observed for mesoionic intermediates BI^- and BI^{-*} that was bounded with a non-classical NHC motif (Figure 1Bi).¹⁰ The low S/T energy gap presumably arose from the considerable repulsion effect between the negative carbon and adjacent oxygen in its singlet state. A triplet state of BI^{-*} was thereby readily accessible from BI⁻ under thermal conditions without photoexcitation. By consideration of this distinct property, a strategy allowing for distal difunctionalization of aldehydes was rationally proposed to afford key biradical intermediates (BR*) upon elimination of the leaving group on the aryl moiety of species BI^{-*} (Figure 1Bii) that was readily formed through its triplet state form under mild conditions.

The envisioned catalytic strategy by harnessing the biradical reactive intermediate from the triplet state of ${\rm BI}^$ was first successfully employed in the reductive defunctionalization of sulfonyl benzaldehydes (Figure 1Ci). Nonclassical triazolium salt pre-NHC A features superior activity in this reaction.¹⁰ Meanwhile, tBuOK as the base was pivotal to giving the free carbene catalyst and deprotonated Breslow intermediate in high efficiency. Alcohol was utilized to trap the eventually produced acyl azolium ions to afford the corresponding benzoate products. The developed redox-neutral hydrodefunctionalization and esterification processes show a broad scope under optimal conditions. A wide range of primary and secondary alcohols, as well as thiols, proceeded smoothly to furnish the desired products (e.g., 2a-2c). Notably, deuterated products were readily afforded when CH₃OD or CD₃OD was employed as the respective nucleophiles (e.g., 2d). Noteworthy is that sulfonyl groups in a more distal site, such as substrate with biaryl moiety, are also capable to give the desulfonylation products. Interestingly, in addition to the sulfonyl units, esters and fluorides are also feasible leaving groups to give the deacetyl (2e) and defluorination esters (2f), respectively, providing an attractive protocol to rapidly assemble the difluoromethylcontaining aromatics.

The developed approach involving the diradical intermediates through the easily accessible triplet state of BI⁻ exhibits great potential in various chemical transformations (Figures 1Bii and 1Biii). For instance, aryl aldehydes with azo functionality 3 were readily transformed into hydrogenated hydrazine products 4 in high yields under the

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Figure 1. Distal difunctionalization of aldehydes through the triplet state of deprotonated Breslow intermediate

(A) Overview of NHC organocatalysis.

(B) Theoretical study and concept of the reaction design.

(C) Representative scope of the distal difunctionalizations.

BI, Breslow intermediate; BR, biradical; ZW, zwitterionic compound.

optimized condition by using methanol as the proton source and nucleophiles (Figure 1Cii). An interesting dearomatization process was observed for anthracene-9-carbaldehyde to give ester product 4c in a modest yield of 32% using the catalytic method. Furthermore, the conditions could be employed in the reduction of the 4-benzoyl to α hydroxylbenzyl group (4d). Another promising application of the diradical process is to explore the C–C bond formations providing opportunities in the construction of molecular complexity. In this context, Liu and co-workers realized an impressive hydro-arylation of alkenes 6 under the NHC catalytic conditions with 4-iodobenzaldehyde 5 in the presence of methanol at 90°C, affording the desired product **7** in 41% yield (Figure 1Ciii).

In summary, this study by Yan and coworkers reveals a low S/T gap of the deprotonated BIs that renders low activation energy of the adducts and the viability for thermal excitation to reach the triplet state of the mesoionic carbene intermediates. In contrast to

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the photo-excited triplet species, the currently developed NHC-bound biradicals feature interesting reactivity toward the tandem distal difunctionalization of aryl aldehydes. This study adds valuable understandings to new NHC-bound radical intermediates and their reactivities. Uncommon transformations via this and similar radical pathways enabled by NHC catalysis can be expected with further development.

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DECLARATION OF INTERESTS

The authors declare no competing interests.

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Metallene pre-catalyst reconstruction for boosting catalytic performance

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In this issue of *Chem Catalysis*, Xu and Zhu's group report the synthesis of novel few-atom-layer stanene quantum dots (Sn-ene QDs) via self-reconstruction of monolayer pre-catalyst, which delivers outstanding performances in CO_2 electroreduction. This research brings promising synthesis strategies of metallene QDs for promoting the industrialization prospect of CO_2 -to-chemicals conversion.

Efficiently converting carbon dioxide (CO_2) into value-added fuels and chemicals is essential to address climate change and rising global energy demand.¹ Electrochemical CO_2 reduction reaction (CO_2RR) presents a promising approach, because it is capable of utilizing intermittent renewable energy

sources to power CO_2 conversion electrolyzers with the generation of carbonneutral products in an environmentally friendly way.² For commercial-scale applications of CO_2RR , however, the conversion efficiency and product selectivity toward target products must be greatly enhanced, which is strongly dependent on proficient electrocatalysts. Therefore, recent research has mainly focused on revealing the catalyst fate during CO₂RR to provide effective guidelines for the newly electrocatalyst design.

Thanks to advanced characterization methods, *in situ* dynamic analysis on electrocatalysts under working conditions has become accessible.^{3–5} Generally speaking, understanding of the realistic reactive surface structures and





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