Chemical Science

EDGE ARTICLE

Cite this: Chem. Sci., 2019, 10, 2501

Advances in reaction development for the stereoselective construction of medicinally important scaffolds or high value-added chemicals depend on utilizing innovative and long-standing synthesis strategies. Over the past decade, a large number of organic transformations driven by N-heterocyclic carbene (NHC) catalysis have been rapidly developed that enabled certain types of reaction manifolds and asymmetric versions of important compounds. Since the seminar report of the Breslow intermediate in 1958, there has been an ever-increasing demand in recruiting novel NHC-bound intermediates for their applications in organic synthesis. Among these achievements, the exploration of NHC-bound enolates for new bond formations has attracted considerable attention from the synthetic community due to its high chemical reactivity and remarkable stereo-control. As shown in Fig. 1a, several readily available starting materials (e.g., enals, aldehydes, ketenes, carboxylic acids, esters) have proven to be effective reactants for the in situ generation of azolium enolates, thus resulting in a large number of distinct reactions and diversified core skeletons. In 2006, Bode et al. first reported an elegant example of the protonation of electron-deficient enals to produce azolium enolates and the subsequent trapping by N-sulfonyl, α,β-unsaturated imines to yield dihydropyridinones. Rovis et al. have pioneered in using α-chloroaldehydes as reactants to prepare azolium enolates for further protonation or internal redox reaction. Meanwhile, Smith et al. also confirmed that α-aryloxyaldehydes as precursors could convert to azolium enolates in NHC-catalyzed redox esterification, amination, and cycloaddition reactions. Moreover, the Smith et al. and Ye

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† Electronic supplementary information (ESI) available. CCDC 1858695. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c8sc04601h

Fig. 1 Representative transformations of azolium enolates catalyzed by NHCs.
et al. have documented that azolium enolates could be readily prepared from ketenes for further annulation. Rovis et al., Chi et al., Scheidt et al., and Ye et al. have utilized aliphatic aldehydes, carboxylic acids, and anhydrides as suit-able reactants to successfully achieve azolium enolates, respectively. In brief, the synthetic utilities of azolium enolates have widely extended to various [2 + 2] [2 + 2] [2 + 2] [2 + 2] cycloadi-ions. These broad diversities may be attributed to the special property of absence of polarity reversal of azolium enolates. Nonetheless, NHC-catalyzed arylation still remains a formidable challenge for synthetic chemists.

Given the success of in situ generated azolium enolates, we anticipated that the desirable NHC-catalyzed arylation reaction might partially be attributed to the looking of suitable substrates. In 2015, Glorius et al. found that the NHC-bound enolates could react with aromatic azomethine imines to generate pyrazolo[3,1-a]isoquinolines via a direct dearomatization process. Inspired by this prominent result, we speculated that a matching electrophile (e.g., electron-deficient aromatic compound) may facilitate the initial dearomatization step via a nucleophilic attack and C–C bond formation, followed by a reaaromatization process, if successfully, to offer the desired arylation molecules (Fig. 1b). We also envisioned that the thermodynamics of this intramolecular cyclodition process probably helps to drive the nucleophilic dearomatization step.

In the process of recruiting suitable substrates, we particu-larly focused on the azobenzene scaffolds because it has the basic required characteristics of being the matching substrate. First, the azobenzene-type structures can be used as electro-philic as well as nucleophilic addition step. Second, the azo group can assist in accomplishing the tandem dearomatization-rearomatization process via intermolecular tautomerization. In fact, azobenzene derivatives as synthons have been broadly utilized in metal-catalyzed transformations, as illustrated by rhodium-catalyzed [3 + 2] cyclization of electron-deficient alkenes with azobenzenes (Fig. 2a). Until recently, the Tan et al. reported an elegant example of chiral phosphoric acid-catalyzed [3 + 2] cyclization of azonaphthalenes with 2,3-disubstituted indoles (Fig. 2b). In these successful examples, the azo motif within the azonaphthalenes not only works as an electron-withdrawing group to activate the aromatic ring, but also plays a critical role in triggering the reaaromatization process. Meanwhile, the NHC-bound enolates, azolium enolate or acyl anions have proven to be effective nucleophiles in catalytic nucleo-phile deaoratization.5,6,13 Inspired by these achievements, we then set out to explore the feasibility of NHC-catalyzed nucleophilic dearomatization of azonaphthalenes with α-chloroaldehyde. Unambiguously, the following challenges need to be overcome in this design: (1) controlling the regioselectivity as the nucleophilic addition of azobenzene derivatives can probably occur at either the N=N double bond or the aromatic ring. (2) Check the compatibility of reactive azonaphthalenes with the nucleophilic NHC-bound enolate intermediates in the deaoratization reaction. (3) Identify the efficient catalytic system for achieving high enantioselectivity. Herein, we report an unprecedented example of NHC-catalyzed α-arylation of azonaphthalenes with α-chloroaldehydes. It should be mentioned that this process contains a formal Csp2-Csp3 bond formation and starts from an organocatalytic nucleophlic aromatic substitution (Fig. 2c).

To validate the feasibility of the hypothesis, our initial reaction development was conducted with α-chloroaldehyde (1a) and azonaphthalene (2a) in the presence of 20 mol% NHC precatalysts and DIPEA in THF at room temperature (Table 1). Only a trace amount or a moderate yield of 3a was achieved using NHC precatalyst A or B (entries 1 and 2). Gratifyingly, the N-Ph-substituted chiral triazolium catalyst (C2) afforded 3a in 72% yield with 90% ee (Table 1, entry 4). Further investigation indicated that the N-2,4,6-(Me)3C6H3- or N-2,6-(Et)3C6H3-substituted chiral triazolium catalyst C1 or C3 gave excellent enantioselectivities, but tolerated moderate yields (entries 3 and 5). Further fine-tuning of other parameters (e.g., base, solvent, and catalyst loading, see ESfor more details) revealed that the optimal condition is a combination of room temperature, 10 mol% C1, 200 mol% DIPEA, and 1.0 mL of t-BuOMe (Table 1, entry 19).

After establishing the optimal reaction conditions, we examined the substrate scope with respect to various α-chloroaldehydes 1 (Fig. 3). The reaction was applicable to α-chloroaldehyde derivatives with either aromatic rings or alkyl chains. The electronic natures or substituted patterns on the aromatic...
ring appeared to have limited effects on reaction results, affording the corresponding dihydrocinnolinones in yields of 73–88% and ee values between 94 and 99% (3a–3i). When the aldehydes containing alkyl R-substituents located at the α-carbon were used, the corresponding dihydrocinnoline derivatives were also afforded with good yields and excellent enantio-controls (3j–3l). Notably, when α-chloroaldehydes bore functional alkyl subunits (e.g., alkene, chlorine, ether) at the side chain, good yields with excellent enantioselectivities were also regularly observed (3m–3r). Pleasingly, 2-chloro-2-phenylacetaldehyde also delivered the corresponding product (3s) in a moderate yield, albeit with a relatively low ee value.

Further investigation on the synthetic feasibility of azonaphthalenes (2) was performed with α-chloroaldehyde (1a), as shown in Fig. 4. The results indicated that this reaction tolerated a diverse array of azonaphthalenes, and afforded the dihydrocinnolinones (4) in good to high yields (76–93%) and with high levels of enantio-controls (93–99% ee). When R’ substituents were alkyl oxide groups (4a–4d), amino group (4e) or sulfonyl group (4f), the products were obtained in high yields with excellent enantioselectivities. Specifically, the electronic nature or the substitution pattern of the aromatic rings showed limited effects on the reactivity (4g–4l). When an anthracene moiety replaced the naphthalene ring in azonaphthalenes, 76% yield and 95% ee were still achieved (4m). The absolute configuration of 3r was determined by single-crystal X-ray diffraction analysis, and those of other products were assigned by analogy.

Furthermore, to demonstrate the practicality of this catalytic transformation, a gram-scale synthesis of 3a was conducted under the optimal condition. There was almost no change in the reaction yield and enantioselectivity (Fig. 5, eqn (1), 90%, 97% ee), implying that the catalytic tandem reaction of...
azonaphthalenes with α-chloroaldehydes can be scaled up. Moreover, the mediated cleavage of 3a mediated by RANEY®-Ni led to the formation of α-substituted chiral amide (5) in 65% yield with the same ee value (Fig. 5, eqn (2)). As illustrated in Scheme 1, a postulated mechanism is described. Initial addition of catalyst C1 to α-chloroaldehyde 1 followed by 1,2-H migration generates NHC-bounded enolate I. Nucleophilic addition of enolate I to azonaphthalene (2) results in a formal tandem reaction of dearomatization and rearomatization along with C–H cleavage and N–H formation to give the thermodynamically stable intermediate III. Finally, intramolecular N-acylation of III leads to the final product 3 or 4 and the NHC catalyst C1 is released for the next catalytic cycle. Surely, a concerted [4 + 2] annulation mechanism cannot be completely ruled out in this case.

In summary, a novel NHC-catalyzed tandem dearomatization/rearomatization reaction of azonaphthalenes with α-chloroaldehydes has been developed. This protocol allows for the rapid assembly of the dihydrocinnolinone scaffolds in good to high yields with high to excellent enantioselectivities. Further investigations on the construction of other relevant frameworks as well as a detailed mechanistic study are currently underway in our laboratory.

**Conflicts of interest**

There are no conflicts to declare.

**Acknowledgements**

Generous financial support for this study was provided by the National Natural Science Foundation of China (No. 21672121, 21871160), the “Thousand Plan” Youth Program of China, the Tsinghua University, the Bayer Investigator fellow, the Fellowship of Tsinghua-Peking Centre for Life Sciences (CLS).

**Notes and references**


2 For selected recent reviews on NHC catalysis: (a) D. Enders, O. Niemeier and A. Henseler, *Chem. Rev.*, 2007, 107, 5606–


19 CCDC 1858695 (3r) contains the supplementary crystallographic data for this paper.†