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Dynamic Kinetic Resolution Enabled by Intramolecular Benzoin Reaction: Synthetic Applications and Mechanistic Insights

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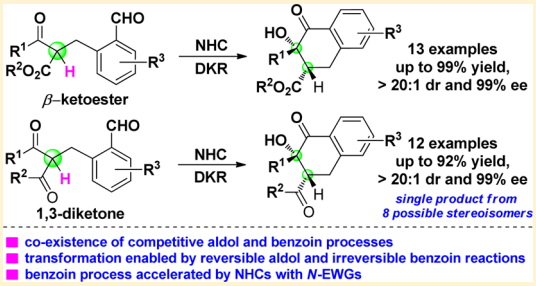
Supporting Information

ABSTRACT: The highly enantio-, diastereo-, and regioselective dynamic kinetic resolution of β-ketoesters and 1,3-diketones was achieved via a chiral *N*-heterocyclic carbene catalyzed intramolecular cross-benzoin reaction. A variety of tetralone derivatives bearing two contiguous stereocenters and multiple functionalities were liberated in moderate to excellent yields and with high levels of stereoselectivity (>95% ee and >20:1 dr in most cases). In addition, the excellent regioselectivity control for aryl/alkyl 1,3-diketones, and the superior electronic differentiation of 1,3-diarylketones were highlighted. Moreover, a set of new mechanistic rationale that differs with the currently widely accepted understanding of intramolecular benzoin reactions was established to demonstrate the superior preference of benzoin over aldol transformation: (1) A coexistence of competitive aldol and benzoin reactions was detected, but a retro-aldol-irreversible benzoin process performs a vital role in the generation of predominant benzoin products. (2) The most essential role of an *N*-electron-withdrawing substituent in triazolium catalysts was revealed to be accelerating the rate of the benzoin transformation, rather than suppressing the aldol process through reducing the inherent basicity of the catalyst.



INTRODUCTION

The asymmetric benzoin reaction enabled by chiral *N*-heterocyclic carbenes (NHCs) has been a longstanding research focus since 1966.[1] The Enders, Rovis, Suzuki, Leeper, You, Cannon, Gravel, and Johnson groups, among others, have made great contributions in this arena through exploiting novel chiral NHC catalysts and discovering innovative benzoin reaction patterns, therefore promoted significantly the development of this named reaction.[2] Since there has been an increasing demand in assembling molecules with stereodiversity and structural complexity in a highly selective and efficient manner both in basic organic research and practical chemical industry, the discovery of protocols allowing access to optically enriched substances with two or more stereocenters via one-step benzoin reaction is thus urgent and indispensable. However, despite the enormous progress being made, it still remains a significant challenge for the current stage of benzoin reactions to address the above issue. In 2009, Ema and co-workers reported the asymmetric desymmetrization of cyclic 1,3-diketones affording bicyclic tertiary alcohols through an intramolecular cross-benzoin reaction.[3] In 2014, Johnson's group disclosed a graceful intermolecular two stereocenters forming benzoin transformation through the dynamic kinetic resolution (DKR)[5] of β-stereogenic α-keto esters.[4] An asymmetric desymmetrization of acyclic 1,3-diketones was also achieved by our group recently.[6] On the basis of these pioneering reports, we envisioned that the introduction of an electron-withdrawing group (EWG) into a ketone-aldehyde substrate (e.g., β-keto ester **1a** and 1,3-diketone **3** in Scheme 1a,c, respectively) should provide a new opportunity in achieving a DKR through an NHC-catalyzed intramolecular benzoin reaction, wherein enantioenriched tetralone products with two stereocenters and multiple functional groups will also be built simultaneously.

However, compared with the previous reports especially those from the Suzuki,[2g,h] Enders,[2f] and You[2i,l] groups, at least two formidable challenges (Scheme 1) must be addressed to achieve an ideal outcomes: (1) The competing aldol-type side reactions must be suppressed. In Suzuki, Ender, and You's early studies, two main strategies were utilized to suppress an aldol process. First, the amounts of base were controlled accurately to be equal to or less than those of the catalysts to minimize aldol side reactions;[2f−i,l,7] second, because the inherent basicity of a free carbene can also promote an aldol process,[2h,8] Suzuki and co-workers modified the NHC catalyst through replacing *N*-phenyl group with an *N*-electron-withdrawing 3,5-$(CF_3)_2C_6H_3$ group and thereby reduced the capability of the catalyst in enolizing substrates.[2h] This approach proved successful, but when substrates with relatively strong acidic protons adjacent to carbonyl groups were utilized, aldol products were still unavoidable (Scheme 1b). For example, in

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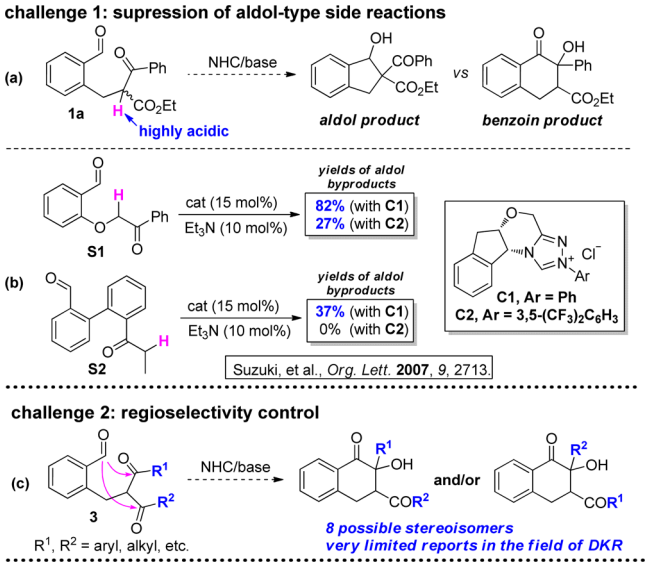
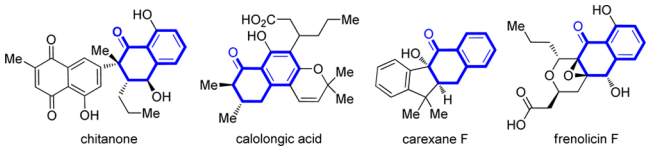
Scheme 1. Key Challenges in Achieving DKR through NHC-Catalyzed Intramolecular Benzoin Reaction



Suzuki's report,[2h] the treatment of **S1** or **S2** with phenyl-substituted Rovis catalyst **C1** afforded aldol-type products in 82 and 37% yields, respectively, although the side reactions can be significantly suppressed by using electron-poor *N*-3,5-$(CF_3)_2C_6H_3$ catalyst **C2**, a 27% combing yield of the byproducts was still obtained when **S1** was tested (Scheme 1b). Thus, considering that the substrates used in this study (e.g., **1a** and **3** in Scheme 1) contain more acidic protons than those in **S1**/**S2** (the K_a value of **1a** is about 4−5 orders of magnitude greater than that of **S1** according to the Bordwell's pK_a table),[9] it can be reasoned that an aldol process should be inevitable and even be predominant.[10] It is also noteworthy that in all the known successful NHC catalysis mediated DKR reports such as those from the Scheidt,[11a] Johnson,[4,11b] and Wang[11c,d] groups excess amounts of base relative to the catalysts were utilized to achieve efficient DKRs, so this contradiction also increases the difficulty of reducing aldol-type byproducts to get an ideal outcome. (2) Furthermore, when 1,3-diketone **3** was employed as the substrate, a new challenge of regioselectivity control during the benzoin reaction arises and must be well-handled besides the diastereo- and enantioselectivity; otherwise, a mixture of maximal eight stereoisomers could be obtained from the benzoin process, thereby making this methodology synthetically useless (Scheme 1c). However, the regiochemistry of the intramolecular benzoin reaction remains an underexploited field thus far; therefore different from the first challenge, no readily available approaches or even hints can be drawn from the currently known reports[1,2] regarding the question about which ketone moiety will be attacked preferentially.

To address all the above challenges, we recently conducted the DKR of ketones with α-EWGs via an intramolecular benzoin reaction. To our delight, through the elaborate screening of reaction conditions, aldol-type side reactions were completely "suppressed", furnishing 1-tetralone products with two contiguous stereocenters in moderate to high yields and with high degrees of stereoselectivity. To be noted, the enantioenriched tetralone products are useful building blocks in organic synthesis and privileged structural motifs in a broad range of natural products and pharmaceuticals (Scheme 2).[12]

Scheme 2. Natural Products Containing Tetralone Units



Furthermore, in contrast to the well-known strategy of trying to suppress aldol reactions to guarantee a smooth benzoin process,[2f−h,7] the mechanistic study of this protocol revealed a competitive aldol process occurring together with the benzoin one, but the reversible aldol and irreversible benzoin processes jointly enabled the formation of the desired products in high yields. Moreover, different from the widely accepted viewpoint,[2h,i,l,n] the most important role of *N*-electron-withdrawing groups in catalysts proved to be not reducing the basicities of catalysts but accelerating the rates of benzoin transformations. All these findings provided a number of new insights into the investigation of the intramolecular benzoin reaction at a fundamental level. Herein we report our results.

RESULTS AND DISCUSSION

As illustrated in Table 1, we commenced by selecting readily available β-ketoester **1a** and a series of aminoindanol-derived carbene catalysts developed initially by the Rovis group to test our hypothesis. Unsurprisingly, aldol product **2a′** was produced predominantly in 76% yield when triazolium **A**[13] (15 mol %) was used as the catalyst and K_2CO_3 (1.0 equiv) was used as the base, and only 10% yield of benzoin product **2a** was obtained, albeit with an excellent diastereoselectivity and a promising 84% ee (Table 1, entry 1). Mesityl-substituted catalyst **B**,[14] first reported by the Bode group, was also tested but gave no better result than that obtained of **A** (Table 1, entry 2). Catalyst **C**, bearing a 4-bromo-phenyl group, induced an excellent ee of 99%; however, the aldol product was still predominant (Table 1, entry 3). The strong electron-withdrawing C_6F_5 group in catalyst **D**[15] proved to be essential in tuning the distribution of products, with benzoin adduct **2a** isolated in 66% yield, but with a low 61% ee (Table 1, entry 4). A variety of chiral catalysts **F**−**I** with diverse skeletons were further examined, and different ratios of benzoin to aldol products were observed with varying degrees of enantioselectivity (Table 1, entries 5−8). To our delight, a search for alternative electron-withdrawing substituents in Rovis type catalysts revealed that triazolium **E**[16] with an *N*-trichlorophenyl group was optimal regarding both the yield (88%) and ee (99%) (Table 1, entry 9). Further effort to suppress the aldol byproduct by evaluating other reaction parameters such as bases and solvents did not lead to better results (Table 1, entries 10−13). We found that lowering the reaction temperature to 0 °C was beneficial to diminish the aldol adduct (Table 1, entry 14). Thus, finally, the optimal result was established by setting the temperature at −20 °C and benzoin product **2a** was produced in almost quantitative yield and with 99% ee (Table 1, entry 15). We note that the use of substoichiometric K_2CO_3 retarded the reaction and led to an increased amount of **2a′** (Table 1, entries 16).

With the optimal conditions in hand, we set out to explore the generality and limitations of this NHC-catalyzed DKR process (Table 2). A variety of aromatic ketones with α-ethoxycarbonyl group performed very well, and both electron-donating and -withdrawing substituents on the aryl rings were tolerated, with extremely excellent 99% ee observed in most

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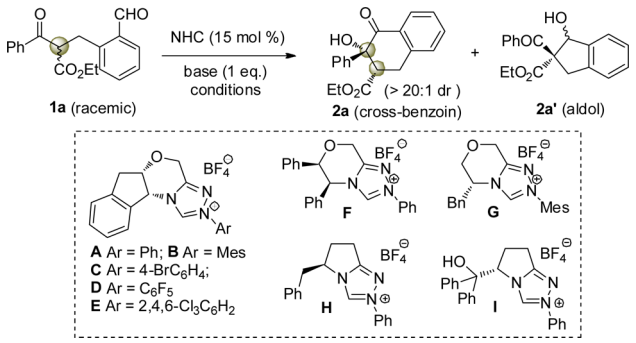
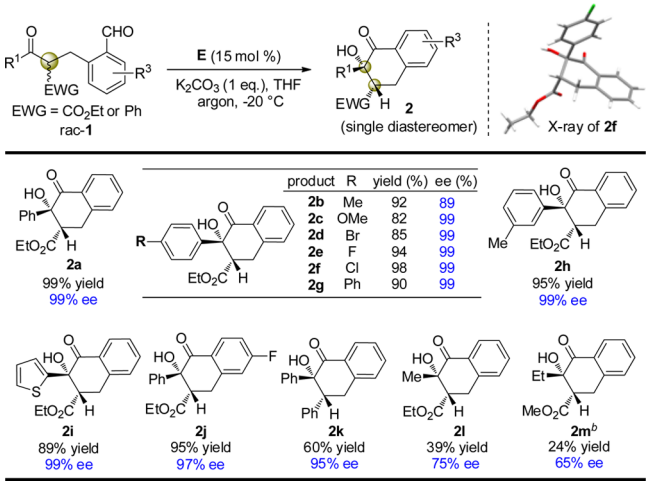
Table 1. Initial Studies and Reaction Optimization[a]



entry	conditions	yield (2a/2a′, %)[b]	ee (2a, %)[c]
1	**A**, K_2CO_3, THF, 23 °C	10/76	84
2	**B**, K_2CO_3, THF, 23 °C	6/53	68
3	**C**, K_2CO_3, THF, 23 °C	8/81	99
4	**D**, K_2CO_3, THF, 23 °C	66/23	61
5	**F**, K_2CO_3, THF, 23 °C	29/51	49
6	**G**, K_2CO_3, THF, 23 °C	42/20	−98
7	**H**, K_2CO_3, THF, 23 °C	25/46	−8
8	**I**, K_2CO_3, THF, 23 °C	1/84	99
9	**E**, K_2CO_3, THF, 23 °C	88/7	99
10	**E**, DIPEA, THF, 23 °C	65/22	99
11	**E**, Cs_2CO_3, THF, 23 °C	72/4	92
12	**E**, K_2CO_3, Toluene, 23 °C	74/6	97
13	**E**, K_2CO_3, CH_2Cl_2, 23 °C	81/5	99
14	**E**, K_2CO_3, THF, 0 °C	90/3	99
15	**E, K_2CO_3, THF, −20 °C**	**99/0**	**99**
16[d]	**E**, K_2CO_3, THF, −20 °C	68/16	99

[a]Reaction conditions: **1a** (0.2 mmol), NHC (15 mol %), solvent (2 mL), base (0.2 mmol), argon protection, 12 h. Diastereomeric ratios were determined via ^{1}H NMR analysis of reaction mixtures. [b]Isolated yields based on **1a**. [c]Determined via HPLC analysis on a chiral stationary phase; the absolute configuration was assigned by analogy to the single-crystal X-ray structure of **2f**.[17] [d]K_2CO_3 (0.75 equiv) was used.

Table 2. Scope of α-Ketoesters[a]

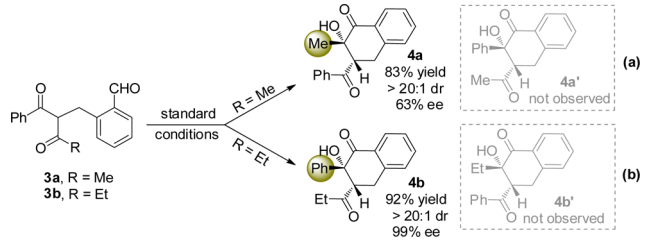


[a]All reactions were run on a 0.2 mmol scale; all yields were of isolated products. In all cases, only one diastereomer was observed via ^{1}H NMR analysis; ee values were determined via HPLC analysis on a chiral stationary phase. The absolute configuration was determined via the X-ray single-crystal structure analysis of **2g**.[17] [b]CH_2Cl_2 was used as the solvent.

cases (Table 2, **2a**–**2h**). Replacement of the phenyl ring at the ketone moiety with a heteroaromatic thienyl group had little effect on the yield (89%) and enantioselectivity (99% ee) (Table 2, **2i**). Introduction of a fluoro substituent into the formylphenyl ring did not encumber the reaction considering both the yield and ee (Table 2, **2j**). The change of electron-withdrawing CO_2Et group to a phenyl group allowed access to the benzoin product with excellent ee (95%), albeit in a moderate yield (Table 2, **2k**). We also surveyed the aliphatic methyl and ethyl ketone substrates and moderate ee (75 and 65%, respectively) was detected (Table 2, **2l** and **2m**). Unfortunately, efforts to expand this protocol to substrates with aliphatic formal groups were not successful; mixtures of two diastereomers were obtained in low yields (<20%) and with low ee (<30%).

Having achieved an efficient DKR of β-ketoesters through the highly selective intramolecular benzoin reaction, we wondered whether this methodology can be extended to 1,3-diketone substrates such as **3a** (Scheme 3). As has been

Scheme 3. Reactions of Me/Ph and Et/Ph 1,3-Diketones



illustrated in Scheme 1c, it is more challenging because besides the resolution efficiency the regioselectivity control is also an arduous mission to be accomplished. It is well-known that regioselective transformations play a vital role in organic synthesis,[18] but to the best of our knowledge, even in the whole domain of asymmetric catalysis, there are very limited successful DKR reports using 1,3-diketones as substrates, most probably owning to the enormous difficulties in controlling the regioselectivity of two similar ketone moieties.[19] Additionally, although regioselectivity study is one of the fundamental aspects in the research field of the intramolecular benzoin reaction, hitherto the related reports are scarcely seen. To test the possibility of achieving the efficient DKR of 1,3-diketones via an intramolecular benzoin reaction, we first examined the reactivity of **3a** under the standard conditions utilized in Table 2. Cheerfully, an excellent regioselectivity was detected, with **4a** as the single benzoin product among eight possible stereomers, albeit with moderate ee; no any other possible isomers such as **4a′** were observed from the ^{1}H NMR analysis of the reaction mixture (Scheme 3a). Moreover, further evaluation of propionyl-substituted **3b** showed a somewhat surprising outcome because **4b** was isolated as the only product, with the phenyl ketone moiety attacked by the acyl anion equivalent (Scheme 3b). It is worthwhile to mention that **4b** was furnished with a high degree of enantioselectivity (99% ee). From the observed results, the regioselectivity sequence in this DKR-mediated intramolecular benzoin reaction can be defined as Me > Ph > Et with respect to the reactivities of ketone units. At the current stage, we speculate that the superposition of both electronic and steric factors of different ketone substituents is responsible for the excellent regioselectivity observed, and the powerfulness of NHC catalysts in

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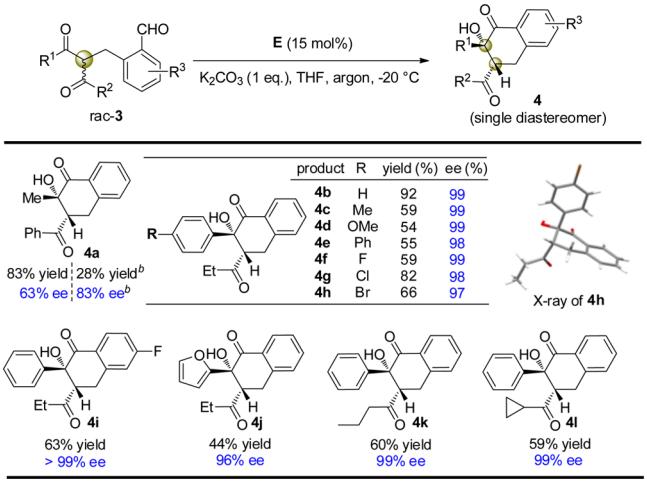
distinguishing minute reactivity differences (such as Me and Et) was distinctly illustrated.[20] More insights into this regioselectivity preference will be one of the focuses in our ongoing investigation.

The scope of this NHC-catalyzed DKR of 1,3-diketones proved very general. First, product **4a** can be gotten with 83% ee under slightly modified conditions using CH_2Cl_2 as the solvent (Table 3, **4a**). Second, variations on the substitution

Table 3. Scope of 1,3-Diketones[a]

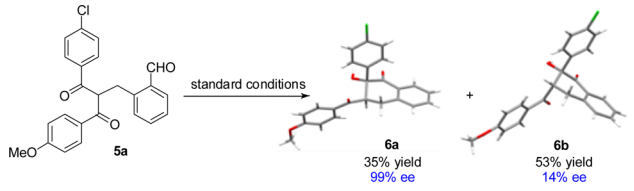


[a]See footnote [a] in Table 2. The absolute configuration was determined via the X-ray single-crystal structure analysis of **4h**.[17] [b]CH_2Cl_2 was used as the solvent.

pattern at the aryl ketone moiety of **2b** were possible. For example, electron-donating Me or OMe groups had little effect on the enantioselectivities (Table 3, **4c**–**4d**); introduction of a phenyl substituent was also amenable, affording **4e** in 55% yield and with excellent 98% ee (Table 3, **4e**). Substrates equipped with electron-withdrawing F, Cl, or Br groups at the para position of the aryl ring were tolerated, releasing the annulation products in moderate to good yields (59–82%) and with excellent enantioselectivities (97–99% ee, Table 3, **4f**–**4h**). The substrate diversity was further evaluated by introducing a fluoro group into the formyl aromatic ring, and no any erosion in enantioselectivity was detected (Table 3, **4i**). A heteroaromatic furyl group substituted ketone was compatible under the standard conditions (Table 3, **4j**). The replacement of the propionyl moiety with a butyryl or cyclopropanecarbonyl group had no significant influence on the regio- and enantioselectivities (99% ee in both cases, Table 3, **4k** and **4l**). It is noteworthy that in all cases the benzoin products were obtained with excellent >20:1 dr, and no any other possible benzoin adducts were perceived.

The substrate scope of this methodology was further expanded to 1,3-diaryketones such as **5a**. To our delight, the subjection of **5a** to the standard conditions exhibited excellent electronic differentiation, with the electron-poor aryl ketone unit being attacked preferentially. However, two diastereomers of **6a** (35% yield, 99% ee) and **6b** (53% yield, 14% ee) were generated, and their structures were confirmed unambiguously via the X-ray crystal analysis[17] (Scheme 4). Disappointingly, attempts to explore the reaction of 1,3-dialkylketones (e.g., Me/Et or Et/cyclopropyl substituted 1,3-diketones) was not successful. Complicated reaction mixtures were obtained, and no possible benzoin products were identified. Anyway, we have

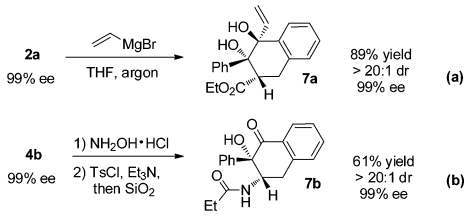
Scheme 4. Reaction of Diaryl-Substituted 1,3-Diketone



provided useful information for the first time with respect to the regiochemistry of the intramolecular benzoin reaction.

To showcase the synthetic applications of this protocol, further transformations based on the enantioenriched benzoin products were performed in highly chemo- and stereoselective manners (Scheme 3). For instance, the diastereoselective nucleophilic attack of chiral **2a** by vinylmagnesium bromide furnished functionalities congested 1,2-diol **7a** in 89% yield and with 99% ee (Scheme 5a).[21] Moreover, the ethyl ketone moiety

Scheme 5. Derivatization of Benzoin Products

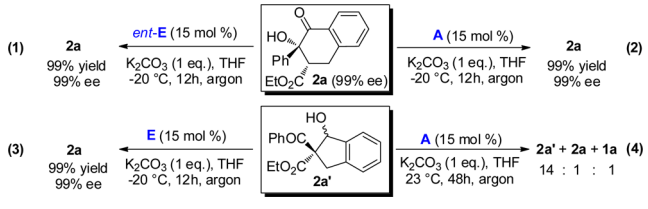


of **4b** underwent the chemoselective reaction with hydroxylamine to form the oxime, and after the Beckmann rearrangement, chiral amide **7b** was delivered without any erosion in enantioselectivity (Scheme 5b).[22]

MECHANISTIC STUDIES

Control Experiments. As has been speculated in the first challenge (Scheme 1a,b) and based on the current understanding of the intramolecular benzoin reaction, an aldol side reaction in this methodology should be inevitable owing to the easily enolizing feature of the substrates under basic conditions. Thus, it is really puzzling because an excellent outcome was obtained in view of the preference of benzoin over aldol transformations. To clarify this perplexity and gain more insights into this highly selective process, we conducted the control experiments depicted in Scheme 6. First, despite the

Scheme 6. Control Experiments



well-known reversible feature of benzoin reactions,[23] the exposure of compound **2a** to the standard conditions with catalyst ***ent*-E** or **A** did not result in any erosion of the ee value or the formation of aldol products, indicating an irreversible benzoin process[24] in this protocol (Scheme 6, eqs 1 and 2). However, the treatment of aldol product **2a′** with trichloro- catalyst **E** led to a full conversion of **2a′** to the benzoin product

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2a under the standard conditions, presumably through a retro-aldol-benzoin process (Scheme 6, eq 3). This result also suggests the possibility of using aldol adducts as aldehyde surrogates to undergo NHC-catalyzed reactions. In contrast to catalyst E, phenyl catalyst A cannot facilitate an aldol to benzoin transformation within 12 h at room temperature, but we did observe the formation of small amounts of benzoin product 2a and starting material 1a in an extended reaction time (48 h), which unambiguously demonstrated the existence of a retro-aldol process[25] (Scheme 6, eq 4).

NMR Monitoring Experiments. Furthermore, to get an intuitive understanding of the reaction profile, we performed NMR tracking experiments through detecting the concentrations of the starting material and the benzoin/aldol products (Figures 1 and 2). The reaction diagram of 1a with trichloro-

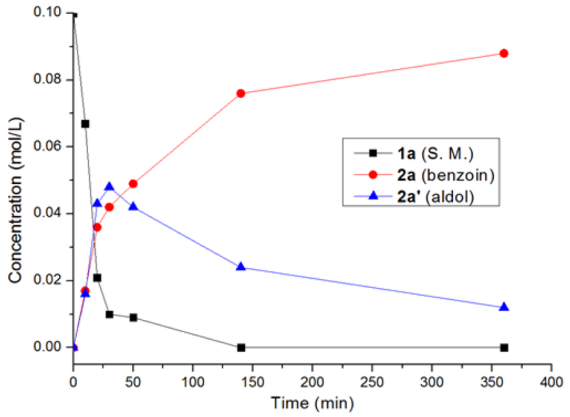


Figure 1. Reaction profile of 1a under the catalysis of E at −20 °C. All conditions were the same as that in Table 2.

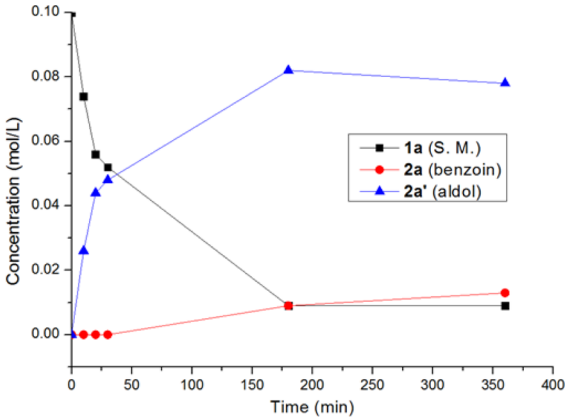
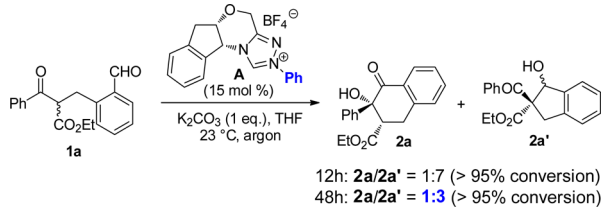


Figure 2. Reaction profile of 1a under the catalysis of A at 23 °C. Other conditions were the same as that in Table 2.

catalyst E (Figure 1) reveals a competitive aldol process against the benzoin one occurring at the initial stage, and then aldol product 2a′ even predominates over benzoin adduct 2a at the point of the 30th minute. Thereafter, 2a′ gradually diminishes accompanied by an increasing amount of 2a, therefore confirming that part of 2a is produced through a retro-aldol-benzoin process (Figure 1).[26] In contrast, the reaction profile of 1a under the catalysis of phenyl-catalyst A (Figure 2) shows a continuous formation of aldol product 2a′ together with a slow generation of 2a in the initial several hours. However, the amount of 2a′ slightly decreases in the sixth hour, accompanied by a small increase in the amount of benzoin product 2a (Figure 2). Hence in both cases, the aldol reactions are absolutely not suppressed, and the main difference between them lies in the rates of the benzoin products formation, with a superior one from catalyst E than that from A. Therefore, entirely distinct from the presently widely accepted and utilized aldol-suppression strategy,[2f−i] a retro-aldol-benzoin process lays the foundation of the success of this intramolecular benzoin reaction.[27]

Evaluation of the Role of N-EWG in the Catalyst. Smith et al. have reported a range of 16.5−18.5 for the pK_a values of triazolium salts with different *N*-substituents in aqueous solution (the pK_a of triazolium A is 16.5; the pK_a of D is 18.5).[28] However, the pK_a values of acetylacetone and ethyl acetoacetate in water are 9.0 and 10.7, respectively.[29] These data indicate that the free carbenes derived from both catalysts A and E have stronger basicities than that from deprotonated 1a; plus with the stoichiometric K_2CO_3 employed in the reaction, we reason that the distinction between A and E in suppressing aldol processes caused by their different basicities should be unconspicuous and therefore were not decisive for the formation of benzoin products in this work. The Smith group has revealed markedly superior rates performed by *N*-electron-deficient aryl triazolium precatalysts than those with *N*-electron-rich substituents in intramolecular Stetter reactions.[30] Bode et al. have also studied comprehensively the reactivity distinction of differently substituted triazoliums.[31] Electron-deficient and sterically more hindered *N*-substituents were considered to be beneficial for the reactivity promotion in acyl anion related reactions.[30,31] On the basis of these important reports and the data depicted in Figures 1 and 2, we concluded that the most important role of an *N*-EWG in catalysts such as E is to enhance the rate of benzoin process to be capable of competing with rather than suppressing the aldol reactions. In contrast, phenyl catalyst A acts on the benzoin reaction in a much slower fashion, caused probably by both the relatively slow Breslow intermediate formation and the sluggish catalyst turnover in the final benzoin product formation step;[30,31] therefore, no remarkable benzoin product can be isolated within the reaction time (12 h). However, it can be reasoned that given enough time the full conversion of 1a to 2a can be realized. ^{1}H NMR analysis of the reaction in Scheme 7

Scheme 7. Reaction of 1a under the Catalysis of A in Different Times



confirmed this deduction: ^{1}H NMR analysis of the reaction mixture showed that the ratio of 2a versus 2a′ increased from 1:7 to 1:3 when the reaction time was extended to 48 h. As a whole, this new finding (i.e., that an *N*-EWG in catalyst is to accelerate the benzoin reaction not to suppress the aldol one) is in sharpest contrast to the intramolecular benzoin reaction related early reports.[2f−i,7]

Proposed Mechanism. On the basis of the above analysis, the mechanistic profile of the whole reaction system can be

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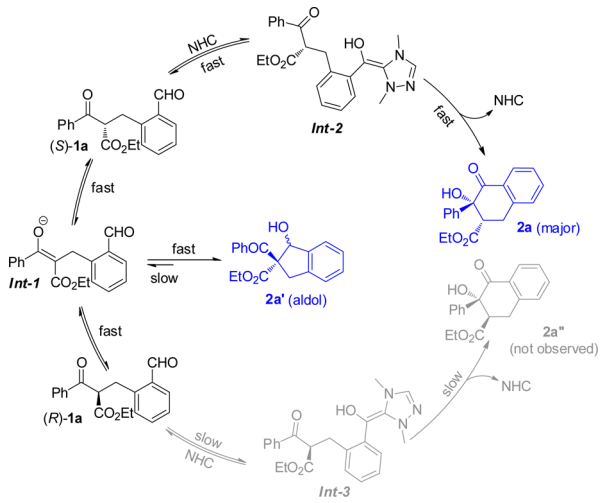
briefly described in Scheme 8. At the initial stage, enoalte **Int-1** is formed in a fast and reversible way from both enantiomers of

Scheme 8. Mechanistic Profile



1a under basic conditions, followed by the rapid release of aldol product **2a′**. Simultaneously, the Breslow intermediate **Int-2** is also generated quickly and reversibly[30] from (*S*)-**1a** and finally affords **2a** via an irreversible benzoin reaction. In contrast, (*R*)-**1a** acts on the NHC catalyst much more slowly; hence, the minor isomer **2a″** was not perceived. Although the retro-aldol step occurs in a slow fashion, it exists throughout the entire dynamic reaction system since the formation of aldol product **2a′**.

CONCLUSIONS

We have demonstrated both the synthetic applications and mechanistic insights of the challenging DKR of α-EWGs substituted ketones enabled by the highly selective intramolecular cross-benzoin reaction for the first time. A variety of enantioenriched tetralones bearing two contiguous stereocenters and multiple functionalities were assembled with high diastereo- and enantioselectivities. In addition, this work shed light on the excellent regioselectivity control for aryl/alkyl 1,3-diketones and the superior electronic differentiation of 1,3-diarylketones. Furthermore, a set of new mechanistic rationale was established to clarify the preference of the benzoin over aldol process: (1) Despite the widely accepted aldol-suppression strategy, a coexistence of both aldol and benzoin reactions was revealed and a retro-aldol-benzoin mechanism enables the generation of benzoin products in a predominant manner. (2) The *N*-electron-withdrawing substituents in NHC catalysts play a vital role in accelerating the transformation of aldehyde-ketone substrates to benzoin products, rather than diminishing aldol products through reducing the basicities of carbene catalysts. Overall, despite the well-known investigations established almost 10 years ago, we provided herein a number of new insights into the fundamental research of the intramolecular benzoin reaction. Further study focusing on the regiochemistry and new reaction modes discovery of the benzoin reaction is ongoing.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.6b02929.

Experimental procedures, spectral data, and crystallographic data (PDF)
Crystallographic information file for compound **2f** (CIF)
Crystallographic information file for compound **2d** (CIF)
Crystallographic information file for compound **6a** (CIF)
Crystallographic information file for compound **6b** (CIF)

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Notes

The authors declare no competing financial interest.

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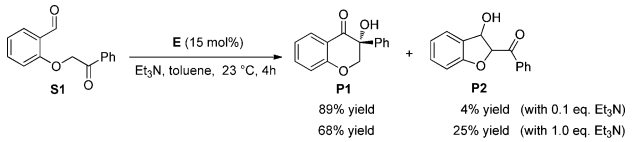

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