OL Organic Letters

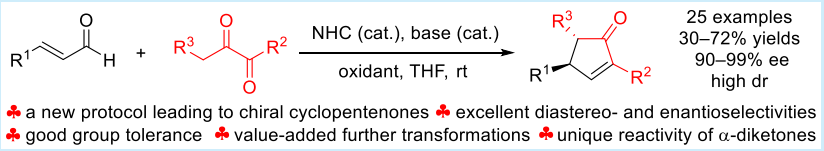
pubs.acs.org/OrgLett Letter

N-Heterocyclic Carbene-Catalyzed Asymmetric Synthesis of Cyclopentenones

Zhizhou Chen, Xiangwen Kong, Shengtong Niu, Shuang Yang,* Jinggong Liu,* Bolai Chen,* Benlong Luo, Changyu Zhou, Chenglin Ding, and Xinqiang Fang*

Cite This: *Org. Lett.* 2021, 23, 3403−3408 Read Online

ACCESS | Metrics & More | Article Recommendations | Supporting Information



ABSTRACT: N-Heterocyclic carbene-catalyzed asymmetric construction of cyclopentenones using enals and α-diketones is achieved, furnishing a series of highly functionalized cyclopentenones in a highly diastereo- and enantioselective manner. The protocol tolerates substrates with both aromatic and aliphatic groups, and further transformations of the products delivered a range of value-added molecules.

Cyclopentenones serve as benchmark substrates for numerous transformations owing to the broad diversity of functionalizations at all five positions on the ring structure that show both nucleophilic and electrophilic reactivities (Figure 1a).[1] Furthermore, the chiral cyclopentenone unit is present in a large number of bioactive compounds such as sesquiterpenes from *Acorus calamus* rhizomes,[2a] (+)-achalensolide,[2b] (−)-terpestacin,[2c,d] przewalskin B,[2e] ainsliadimer B,[2f] etc. (Figure 1b). Therefore, a large number of reactions have been reported to make chiral cyclopentenones, which have been well documented in a series of reviews.[3]

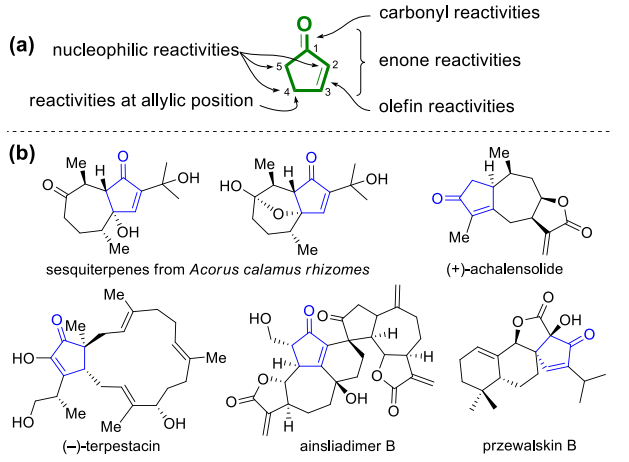


Figure 1. Reactivities of cyclopentenones and natural products containing cyclopentenone units.

However, a detailed literature survey shows that most of the methods rely on the resolution of racemic cyclopentenones,[4a] asymmetric functionalization of existing cyclopentenone units,[4b] and modifications on chiral building blocks;[4c] protocols allowing the direct construction of cyclopentenone rings via asymmetric catalysis remain underdeveloped. In this context, transition-metal-catalyzed asymmetric Pauson−Khand reaction[5a−e] and Nazarov cyclization[5f−i] represent two types of the most commonly studied approaches for achieving the purpose described above. In sharp contrast, organocatalyzed asymmetric cyclopentenone synthesis has been scarcely realized. BINOL-*N*-triflyl phosphoramides have been employed to catalyze the asymmetric Nazarov cyclizations by Nachtsheim, Rueping, and Ieawsuwan et al.[6] Jørgensen and coworkers described a two-step method using both secondary amine and N-heterocyclic carbene (NHC) as the catalysts to afford chiral cyclopentenones.[7] Considering the high importance of chiral cyclopentenones and the currently limited approaches for directly contructing cyclopentenone rings in asymmetric fashions, the development of new methods is still urgently needed.

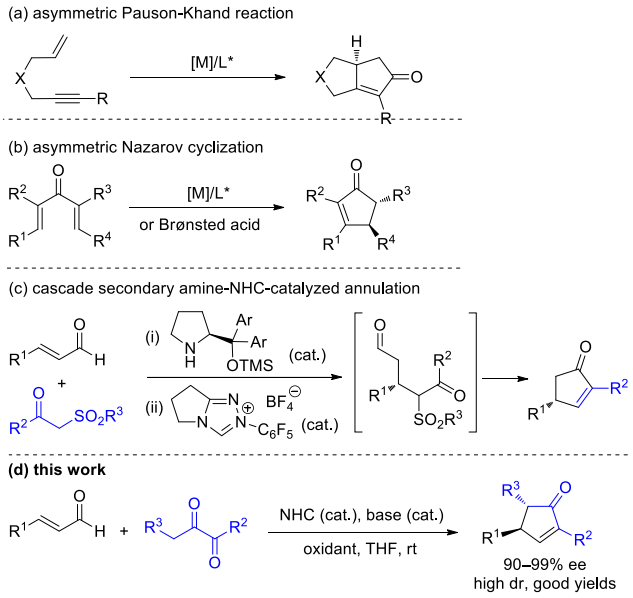
We have commenced a systematic study of α-diketone chemistry and revealed a series of unique reactivities of α-diketones.[8] On the other hand, oxidative NHC catalysis has been a robust strategy in the asymmetric construction of cyclic molecules.[9] Here we report that α-diketone substrates can be used as nucleophilic reagents to perform cascade annulations

Received: March 12, 2021
Published: April 12, 2021

https://doi.org/10.1021/acs.orglett.1c00870
Org. Lett. 2021, 23, 3403−3408

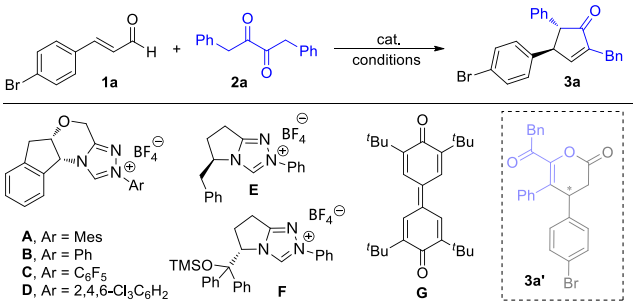
under oxidative NHC catalysis to release a series of highly functionalized cyclopentenones in an excellent diastereo- and enanantioselective manner. The mechanism of cyclopentenone formation is thoroughly different from that of Jørgensen's report,[7] and to the best of our knowledge, such an annulation mode has not been disclosed in the realm of NHC catalysis.[9] Therefore, this work provides a new choice of direct and asymmetric construction of cyclcopentenone rings. Herein, we report the results (Scheme 1).

Scheme 1. Catalytic Asymmetric Construction of Cyclopentenones



First, we selected *trans*-4-bromocinnamaldehyde **1a**, diketone **2a**, and NHC **A** to optimize the reaction conditions. To our delight, cyclopentenone **3a** was isolated as a single diastereoisomer in 62% yield with excellent 93% ee using K_2CO_3 as the base, THF as the solvent, and **G** as the oxidant (Table 1, entry 1). It is noteworthy that possible byproduct lactone **3a′**, whose formation has been well documented in literature reports via α,β-unsaturated acyl azoliums,[10] was not observed. Then we tested a series of amino indanol-derived catalysts, such as **B**–**D**, but in these cases, only a minimal amount of **3a** was formed (Table 1, entries 2–4, respectively). Catalysts **E** and **F** showed similar results (Table 1, entries 5 and 6, respectively). Using catalyst **A**, we further tested a series of bases such as $NaHCO_3$, Et_3N, Cs_2CO_3, ^tBuOK, and DBU, but only inferior results were observed (Table 1, entries 7–11, respectively). We then evaluated different solvents (i.e., toluene and CH_2Cl_2) while using K_2CO_3 as the base, but lower yields were detected (Table 1, entries 12 and 13, respectively). Gratifyingly, increasing the amount of both triazolium **A** and K_2CO_3 to 20 mol % could enhance the yields without affecting the enantioselectivity (Table 1, entry 14). Then the yield of **3a** was increased to 70% upon addition of slightly more oxidant (Table 1, entry 15). We also tested the reaction without an NHC catalyst and isolated a 14% yield of **3a**, indicating that background reaction also occurs (Table 1, entry 16). The reactions without K_2CO_3 or with 10 mol % K_2CO_3 also occurred but delivered **3a** in lower yields (entries 17 and 18).

Table 1. Optimization of Reaction Conditions[a]



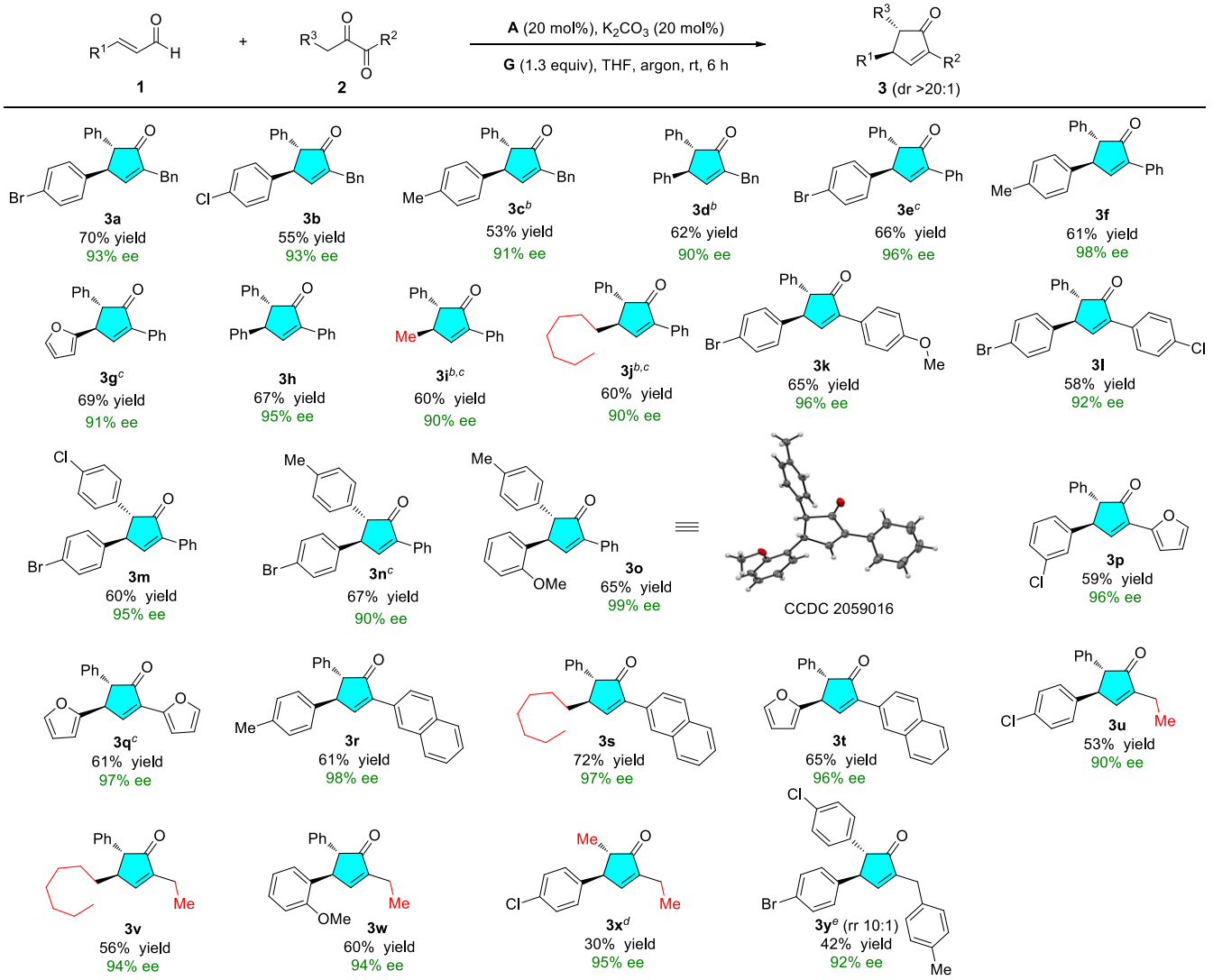
entry	catalyst	base	solvent	time (h)	yield (%)[b]	ee (%)[c]
1	**A**	K_2CO_3	THF	1	62	93
2	**B**	K_2CO_3	THF	1	17	82
3	**C**	K_2CO_3	THF	1	trace	–
4	**D**	K_2CO_3	THF	1	trace	–
5	**E**	K_2CO_3	THF	1	trace	–
6	**F**	K_2CO_3	THF	1	trace	–
7	**A**	$NaHCO_3$	THF	1	trace	–
8	**A**	Et_3N	THF	1	trace	–
9	**A**	Cs_2CO_3	THF	1	53	89
10	**A**	^tBuOK	THF	1	51	87
11	**A**	DBU	THF	1	38	86
12	**A**	K_2CO_3	toluene	1	15	90
13	**A**	K_2CO_3	CH_2Cl_2	1	38	92
14[d,e]	**A**	K_2CO_3	THF	6	68	91
15[d–f]	**A**	K_2CO_3	THF	6	70	93
16[d,f]	–	K_2CO_3	THF	6	14	–
17[e,f]	**A**	–	THF	6	61	92
18[e,f]	**A**	K_2CO_3	THF	6	57	93

[a]Reaction conditions: **1a** (0.2 mmol), **2a** (0.24 mmol), base (0.02 mmol), solvent (1 mL), catalyst (0.02 mmol), **G** (0.2 mmol), under argon protection, rt. [b]Isolated yields based on **1a**. [c]Determined via HPLC analysis on a chiral stationary phase. [d]Base (0.04 mmol) was added. [e]Catalyst **A** (0.04 mmol) was used. [f]**G** (0.26 mmol) was added.

Having identified the optimal conditions, we then evaluated the substrate scope to demonstrate the generality and limitation of this transformation (Scheme 2). Using benzyl diketone **2a** as the nucleophile, a series of differently substituted aromatic enals were examined. We found that the reaction could tolerate enals with 4-ClC_6H_4, Ph, and electron-donating 4-MeC_6H_4 substituents, delivering the corresponding products with excellent 90–93% ee in moderate to good yields (Scheme 2, **3b**–**3d**, respectively). Then we turned our attention to unsymmetrical diketones such as benzyl/phenyl diketone **2b**. The variation of the R^1 group from electron-withdrawing 4-BrC_6H_4 to Ph, heterocyclic furan, or electron-donating 4-MeC_6H_4 all proved successful, and the cyclopentenones could be obtained with ≤98% ee (Scheme 2, **3e**–**3h**). When R^1 was methyl or ^{n}heptyl groups, the reaction also proceeded well to release the corresponding products with 90% ee (Scheme 2, **3i** and **3j**). Then using *trans*-4-bromocinnamaldehyde **1a** as a substrate, we evaluated a series of differently substituted benzyl/phenyl diketones and found that the substituents installed in the phenyl group had little impact on the reactions (Scheme 2, **3k**–**3n**). It is noteworthy that the reaction of the 2-$MeOC_6H_4$-substituted enal with the diketone could also provide the annulation product in 65% yield with excellent 99% ee (Scheme 2, **3o**). Furthermore, the

https://doi.org/10.1021/acs.orglett.1c00870
Org. Lett. 2021, 23, 3403–3408

Scheme 2. Substrate Scope[a]



[a]All reactions were run on a 0.2 mmol scale. ee values were determined via HPLC analysis on a chiral stationary phase. All yields were of isolated products. [b]The reaction mixture was held at −10 to 0 °C for 7−18 h. [c]**B** (0.04 mmol) was used instead of **A**. [d]dr = 10:1. [e]The reaction was performed at 0 °C, and the regioselectivity was 10:1.

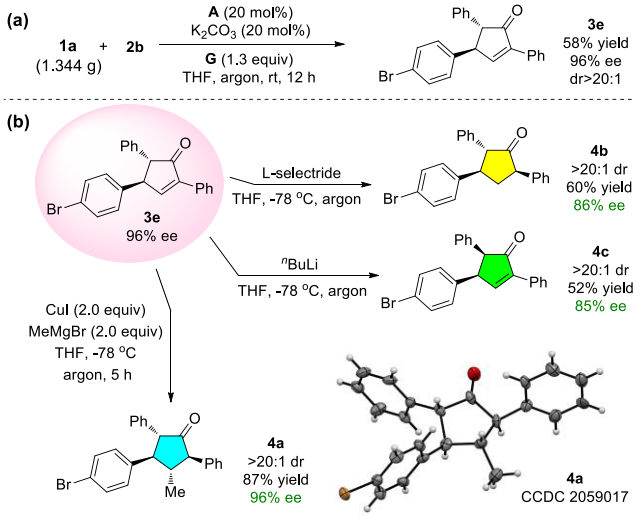
variation of both R^1 and R^2 groups proved feasible, and the substrates having different substitution patterns all reacted well to produce the corresponding products with ≤98% ee in moderate to good yields (Scheme 2, **3p**−**3w**). It is worth mentioning that only one diastereoisomer was detected in all of the cases mentioned above. A diketone substrate with two aliphatic substituents was also tested, and the cyclopentenone product could be obtained with 95% ee, albeit in diminished yield (Scheme 2, **3x**). Regioselective annulation using differently substituted dibenzyl type diketone could also be achieved, leading to **3y** in 42% yield with 92% ee (Scheme 2, **3y**). The relative configuration of **3o** was determined by single-crystal X-ray analysis, and other products were assigned by analogy.

The scale-up reaction can be realized using 1.344 g of **1a**, affording **3e** in 58% yield without erosion of the enantioselectivity (Scheme 3a). Moreover, the optically enriched cyclopentenone product prepared by our catalytic annulation reaction could readily undergo further transformations (Scheme 3b). For instance, the nucleophilic attack of **3e** by methyl copper reagent could provide cyclopentanone **4a** in good yield with high enantioselectivity. It is noteworthy that **4a** contains four adjacent stereocenters, and the configuration of **4a** was confirmed by single-crystal X-ray analysis. Furthermore, L-selectride reduction of **3e** afforded **4b** in 60% yield, and the relative configuration was confirmed via NOESY spectrum analysis.[11] Interestingly, the *trans*-cyclopentenone product could be converted to *cis*-product **4c** in moderate yield with high ee when strong base ^{n}BuLi was used.[12]

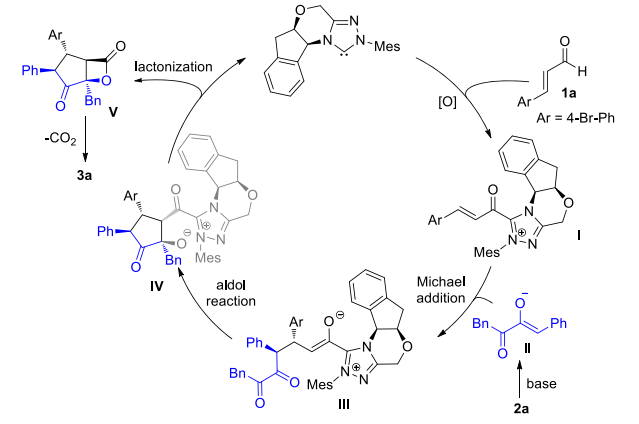
A probable mechanism for the construction of cyclopentenone is shown in Scheme 4. The reaction of a carbene catalyst with enal under the oxidative conditions affords azolium **I**; meanwhile, enolate **II** is produced from diketone **2a** under basic conditions. A Michael addition of **II** to **I** produces intermediate **III**, which is followed by an intramolecular aldol reaction−lactonization sequence to produce lactone **V**. Then after the decarboxylation, cyclopentenone **3a** is finally obtained. Attempts to detect or trap lactone **V** using a mixed

https://doi.org/10.1021/acs.orglett.1c00870
Org. Lett. 2021, 23, 3403−3408

Scheme 3. Scale-up Reaction and Synthetic Applications of the Products



Scheme 4. Postulated Mechanism



solvent of THF and MeOH all failed, which indicate that the decarboxylation and formation of **3a** is a fast process.

In conclusion, starting from enals and diketones, we have successfully achieved the asymmetric construction of highly functionalized cyclopentenones using NHC organocatalysis. The protocol affords a variety of cyclopentenones bearing two stereocenters with excellent diastereo- and enantioselectivities. The reaction mode is thoroughly different from the conventional one using NHC catalysis that leads to dihydropyranone products. A series of valuable transformations using the enantioenriched cyclopentenones can be readily achieved, allowing access to various value-added synthetic building blocks. The work also demonstrates the great potential of 1,2-diketone compounds in the discovery of new reaction modes.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.orglett.1c00870.

Experimental procedures, spectroscopic data for all new compounds, and crystallographic data for **3o** and **4a** (PDF)

Accession Codes

CCDC 2059016−2059017 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

■ AUTHOR INFORMATION

Corresponding Authors

Xinqiang Fang − *College of Chemistry, Fuzhou University, Fuzhou 350116, China; State Key Laboratory of Structural Chemistry and Key Laboratory of Coal to Ethylene Glycol and Its Related Technology, Center for Excellence in Molecular Synthesis, Fujian Institute of Research on the Structure of Matter, University of Chinese Academy of Sciences, Fuzhou 350100, China;* orcid.org/0000-0001-8217-7106; Email: xqfang@fjirsm.ac.cn

Shuang Yang − *State Key Laboratory of Structural Chemistry and Key Laboratory of Coal to Ethylene Glycol and Its Related Technology, Center for Excellence in Molecular Synthesis, Fujian Institute of Research on the Structure of Matter, University of Chinese Academy of Sciences, Fuzhou 350100, China*; Email: yangshuang@fjirsm.ac.cn

Bolai Chen − *Orthopedics Department, Guangdong Provincial Hospital of Traditional Chinese Medicine, Guangzhou 510120, China*; Email: chenbolai337@163.com

Jinggong Liu − *Orthopedics Department, Guangdong Provincial Hospital of Traditional Chinese Medicine, Guangzhou 510120, China*; Email: liujinggong001@163.com

Authors

Zhizhou Chen − *College of Chemistry, Fuzhou University, Fuzhou 350116, China*

Xiangwen Kong − *State Key Laboratory of Structural Chemistry and Key Laboratory of Coal to Ethylene Glycol and Its Related Technology, Center for Excellence in Molecular Synthesis, Fujian Institute of Research on the Structure of Matter, University of Chinese Academy of Sciences, Fuzhou 350100, China*

Shengtong Niu − *State Key Laboratory of Structural Chemistry and Key Laboratory of Coal to Ethylene Glycol and Its Related Technology, Center for Excellence in Molecular Synthesis, Fujian Institute of Research on the Structure of Matter, University of Chinese Academy of Sciences, Fuzhou 350100, China*

Benlong Luo − *Pingxiang University, Pingxiang 337055, China*

Changyu Zhou − *College of Chemistry, Fuzhou University, Fuzhou 350116, China*

Chenglin Ding − *College of Chemistry, Fuzhou University, Fuzhou 350116, China*

Complete contact information is available at: https://pubs.acs.org/10.1021/acs.orglett.1c00870

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This work was supported by the NSFC (21871260 and 22071242), the Strategic Priority Research Program of the

Chinese Academy of Sciences (XDB20000000), and the Science and Technology Research Program of the Education Department of Jiangxi Province (GJJ1991151).

REFERENCES

(1) For selected reviews, see: (a) Poplata, S.; Tröster, A.; Zou, Y.-Q.; Bach, T. Recent Advances in the Synthesis of Cyclobutanes by Olefin [2 + 2] Photocycloaddition Reactions. *Chem. Rev.* **2016**, *116*, 9748−9815. (b) Touré, B. B.; Hall, D. G. Natural Product Synthesis Using Multicomponent Reaction Strategies. *Chem. Rev.* **2009**, *109*, 4439−4486. (c) Klunder, A. J. H.; Zhu, J.; Zwanenburg, B. The Concept of Transient Chirality in the Stereoselective Synthesis of Functionalized Cycloalkenes Applying the Retro-Diels−Alder Methodology. *Chem. Rev.* **1999**, *99*, 1163−1190.

(2) (a) Hao, Z. Y.; Liang, D.; Luo, H.; Liu, Y. F.; Ni, G.; Zhang, Q. J.; Li, L.; Si, Y. K.; Sun, H.; Chen, R. Y.; Yu, D. Q. Bioactive Sesquiterpenoids from the Rhizomes of *Acorus calamus*. *J. Nat. Prod.* **2012**, *75*, 1083−1089. (b) Sainte-Luce Banchelin, T.; Carret, S.; Giannini, A.; Deprés, J.-P. Short and Stereoselective Total Synthesis of Δ-11,13-Didehydroguaianes and -guaianolides: Synthesis of (±)-Achalensolide and (±)-Pechueloic Acid; Revision of the Structure of (+)-Rupestonic Acid. *Eur. J. Org. Chem.* **2009**, *2009*, 3678−3682. (c) Jin, Y. H.; Qiu, F. Y. G. A Convergent Stereocontrolled Total Synthesis of (−)-Terpestacin. *Org. Biomol. Chem.* **2012**, *10*, 5452−5455. (d) Jung, H. J.; Shim, J. S.; Lee, J.; Song, Y. M.; Park, K. C.; Choi, S. H.; Kim, N. D.; Yoon, J. H.; Mungai, P. T.; Schumacker, P. T.; Kwon, H. J. Terpestacin Inhibits Tumor Angiogenesis by Targeting UQCRB of Mitochondrial Complex III and Suppressing Hypoxia-Induced Reactive Oxygen Species Production and Cellular Oxygen Sensing. *J. Biol. Chem.* **2010**, *285*, 11584−11595. (e) Xu, G.; Hou, A. J.; Zheng, Y. T.; Zhao, Y.; Li, X. L.; Peng, L. Y.; Zhao, Q. S. Przewalskin B, a Novel Diterpenoid with an Unprecedented Skeleton from Salvia przewalskii Maxim. *Org. Lett.* **2006**, *9*, 291−293. (f) Li, C.; Dian, L.; Zhang, W.; Lei, X. Biomimetic Syntheses of (−)-Gochnatiolides A−C and (−)-Ainsliadimer B. *J. Am. Chem. Soc.* **2012**, *134*, 12414−12417.

(3) For selected reviews, see: (a) Simeonov, S. P.; Nunes, J. P. M.; Guerra, K.; Kurteva, V. B.; Afonso, C. A. M. Synthesis of Chiral Cyclopentenones. *Chem. Rev.* **2016**, *116*, 5744−5893. (b) Aitken, D.; Eijsberg, H.; Frongia, A.; Ollivier, J.; Piras, R. P. Recent Progress in the Synthetic Assembly of 2-Cyclopentenones. *Synthesis* **2013**, *46*, 1−24. (c) Roche, S. P.; Aitken, D. J. Chemistry of 4-Hydroxy-2-cyclopentenone Derivatives. *Eur. J. Org. Chem.* **2010**, *2010*, 5339−5358. (d) Gibson, S. E.; Lewis, S. E.; Mainolfi, N. Transition Metal-Mediated Routes to Cyclopentenones. *J. Organomet. Chem.* **2004**, *689*, 3873−3890. (e) Ellison, R. A. Methods for the Synthesis of 3-Oxocyclopentenes. *Synthesis* **1973**, *1973*, 397−412. (f) Piancatelli, G.; D'Auria, M.; D'Onofrio, F. Synthesis of 1,4-Dicarbonyl Compounds and Cyclopentenones from Furans. *Synthesis* **1994**, *1994*, 867−889.

(4) For selected reports, see: (a) Wang, Y.; Feng, X.; Du, H. Kinetic Resolution of Hindered Morita-Baylis-Hillman Adducts by Rh(I)-Catalyzed Asymmetric 1,4-Addition/β-Hydroxyelimination. *Org. Lett.* **2011**, *13*, 4954−4957. (b) Deng, Q.-H.; Wadepohl, H.; Gade, L. H. Highly Enantioselective Copper-Catalyzed Alkylation of β-Ketoesters and Subsequent Cyclization to Spirolactones/Bi-spirolactones. *J. Am. Chem. Soc.* **2012**, *134*, 2946−2949. (c) Choi, W. J.; Moon, H. R.; Kim, H. O.; Yoo, B. N.; Lee, J. A.; Shin, D. H.; Jeong, L. S. Preparative and Stereoselective Synthesis of the Versatile Intermediate for Carbocyclic Nucleosides: Effects of the Bulky Protecting Groups to Enforce Facial Selectivity. *J. Org. Chem.* **2004**, *69*, 2634−2636.

(5) (a) Ingate, S. T.; Marco-Contellers, J. The Asymmetric Pauson-Khand Reaction. A Review. *Org. Prep. Proced. Int.* **1998**, *30*, 121−143. (b) Shibata, T. Recent Advances in the Catalytic Pauson-Khand-Type Reaction. *Adv. Synth. Catal.* **2006**, *348*, 2328−2336. (c) Jeong, N.; Sung, B. K.; Choi, Y. K. Rhodium(I)-Catalyzed Asymmetric Intramolecular Pauson-Khand-Type Reaction. *J. Am. Chem. Soc.* **2000**, *122*, 6771−6772. (d) Shibata, T.; Takagi, K. Iridium-Chiral Diphosphine Complex Catalyzed Highly Enantioselective Pauson-Khand-Type Reaction. *J. Am. Chem. Soc.* **2000**, *122*, 9852−9853. (e) Kwong, F. Y.; Li, Y. M.; Lam, W. H.; Qiu, L.; Lee, H. W.; Yeung, C. H.; Chan, K. S.; Chan, A. S. C. Rhodium-Catalyzed Asymmetric Aqueous Pauson-Khand-Type Reaction. *Chem. - Eur. J.* **2005**, *11*, 3872−3880. (f) Kawatsura, M.; Kajita, K.; Hayase, S.; Itoh, T. Iron- or Cobalt-Catalyzed Nazarov Cyclization: Asymmetric Reaction and Tandem Cyclization-Fluorination Reaction. *Synlett* **2010**, *2010*, 1243−1246. (g) Liang, G.; Trauner, D. Enantioselective Nazarov Reactions Through Catalytic Asymmetric Proton Transfer. *J. Am. Chem. Soc.* **2004**, *126*, 9544−9545. (h) Cao, P.; Deng, C.; Zhou, Y. Y.; Sun, X. L.; Zheng, J. C.; Xie, Z.; Tang, Y. Asymmetric Nazarov Reaction Catalyzed by Chiral Tris-(oxazoline)/Copper(II). *Angew. Chem., Int. Ed.* **2010**, *49*, 4463−4466. (i) Xu, Z.; Ren, H.; Wang, L.; Tang, Y. Efficient Catalytic Enantioselective Nazarov Cyclizations of Divinyl Ketoesters. *Org. Chem. Front.* **2015**, *2*, 811−814. (j) Komatsuki, K.; Kozuma, A.; Saito, K.; Yamada, T. Decarboxylative Nazarov Cyclization-Based Chirality Transfer for Asymmetric Synthesis of 2-Cyclopentenones. *Org. Lett.* **2019**, *21*, 6628−6632.

(6) (a) Rueping, M.; Ieawsuwan, W.; Antonchick, A. P.; Nachtsheim, B. J. Chiral Bronsted Acids in the Catalytic Asymmetric Nazarov Cyclization-the First Enantioselective Organocatalytic Electrocyclic Reaction. *Angew. Chem., Int. Ed.* **2007**, *46*, 2097−2100. (b) Rueping, M.; Ieawsuwan, W. A Catalytic Asymmetric Electrocyclization-Protonation Reaction. *Adv. Synth. Catal.* **2009**, *351*, 78−84. (c) Raja, S.; Ieawsuwan, W.; Korotkov, V.; Rueping, M. Asymmetric Brønsted Acid-Catalyzed Nazarov Cyclization of Acyclic α-Alkoxy Dienones. *Chem. - Asian J.* **2012**, *7*, 2361−2366.

(7) Jacobsen, C. B.; Jensen, K. L.; Udmark, J.; Jorgensen, K. A. Organocatalytic Iminium Ion/Carbene Reaction Cascade for the Formation of Optically Active 2,4-Disubstituted Cyclopentenones. *Org. Lett.* **2011**, *13*, 4790−4793.

(8) (a) Liu, J.; Das, D. K.; Zhang, G.; Yang, S.; Zhang, H.; Fang, X. N-Heterocyclic Carbene-Catalyzed Umpolung of β,γ-Unsaturated 1,2-Diketones. *Org. Lett.* **2018**, *20*, 64−67. (b) Li, X.; Kong, X.; Yang, S.; Meng, M.; Zhan, X.; Zeng, M.; Fang, X. Bifunctional Thiourea-Catalyzed Asymmetric Inverse-Electron-Demand Diels-Alder Reaction of Allyl Ketones and Vinyl 1,2-Diketones via Dienolate Intermediate. *Org. Lett.* **2019**, *21*, 1979−1983. (c) Nagaraju, S.; Liu, S.; Liu, J.; Yang, S.; Liu, R.; Chen, Z.; Paplal, B.; Fang, X. Regioselectivity-Switchable Catalytic Annulations of Alkynyl α-Diketones and α-Cyanoketones. *Org. Lett.* **2019**, *21*, 10075−10080. (d) Liu, W.; Niu, S.; Zhao, Z.; Yang, S.; Liu, J.; Li, Y.; Fang, X. Divergent Synthesis of Bicyclo[3.2.1]octenes and Cyclohexenes via Catalytic Annulations of Nazarov Reagent and Vinyl 1,2-Diketones. *Org. Lett.* **2020**, *22*, 7572−7576.

(9) For selected reviews, see: (a) Enders, D.; Niemeier, O.; Henseler, A. Organocatalysis by N-Heterocyclic Carbenes. *Chem. Rev.* **2007**, *107*, 5606−5655. (b) Biju, A. T.; Kuhl, N.; Glorius, F. Extending NHC-Catalysis: Coupling Aldehydes with Unconventional Reaction Partners. *Acc. Chem. Res.* **2011**, *44*, 1182−1195. (c) Bugaut, X.; Glorius, F. Organocatalytic Umpolung: N-Heterocyclic Carbenes and Beyond. *Chem. Soc. Rev.* **2012**, *41*, 3511−3522. (d) Ryan, S. J.; Candish, L.; Lupton, D. W. Acyl Anion Free N-Heterocyclic Carbene Organocatalysis. *Chem. Soc. Rev.* **2013**, *42*, 4906−4917. (e) Flanigan, D. M.; Romanov-Michailidis, F.; White, N. A.; Rovis, T. Organocatalytic Reactions Enabled by N-Heterocyclic Carbenes. *Chem. Rev.* **2015**, *115*, 9307−9387. (f) Murauski, K. J. R.; Jaworski, A. A.; Scheidt, K. A. A Continuing Challenge: N-Heterocyclic Carbene-Catalyzed Syntheses of γ-Butyrolactones. *Chem. Soc. Rev.* **2018**, *47*, 1773−1782. (g) Chen, X.; Wang, H.; Jin, Z.; Chi, Y. R. N-Heterocyclic Carbene Organocatalysis: Activation Modes and Typical Reactive Intermediates. *Chin. J. Chem.* **2020**, *38*, 1167−1202. (h) Ren, Q.; Li, M.; Yuan, L.; Wang, J. Recent Advances on N-heterocyclic Carbene Catalyzed Achiral Synthesis. *Org. Biomol. Chem.* **2017**, *15*, 4731−4749. For a selected report, see: (i) Lathrop, S. P.; Rovis, T. Asymmetric Synthesis of Functionalized Cyclopentanones via a Multicatalytic Secondary Amine/N-Heterocyclic Carbene Catalyzed Cascade Sequence. *J. Am. Chem. Soc.* **2009**, *131*, 13628−13630.

https://doi.org/10.1021/acs.orglett.1c00870
Org. Lett. 2021, 23, 3403−3408

(10) For selected reviews of α,β-unsaturated acyl azoliums, see: (a) De Sarkar, S.; Biswas, A.; Samanta, R. C.; Studer, A. Catalysis with N-Heterocyclic Carbenes under Oxidative Conditions. *Chem. - Eur. J.* **2013**, *19*, 4664−4678. (b) Ryan, S. J.; Candish, L.; Lupton, D. W. Acyl Anion Free N-Heterocyclic Carbene Organocatalysis. *Chem. Soc. Rev.* **2013**, *42*, 4906−4917. (c) Mahatthananchai, J.; Bode, J. W. On the Mechanism of N-Heterocyclic Carbene-Catalyzed Reactions Involving Acyl Azoliums. *Acc. Chem. Res.* **2014**, *47*, 696−707. (d) Levens, A.; Lupton, D. W. All-Carbon (4 + 2) Annulations Catalysed by N-Heterocyclic Carbenes. *Synlett* **2017**, *28*, 415−424. (e) Zhang, C.; Hooper, J. F.; Lupton, D. W. N-Heterocyclic Carbene Catalysis via the α,β-Unsaturated Acyl Azolium. *ACS Catal.* **2017**, *7*, 2583−2596. (f) Mondal, S.; Yetra, S. R.; Mukherjee, S.; Biju, A. T. NHC-Catalyzed Generation of α,β-Unsaturated Acylazoliums for the Enantioselective Synthesis of Heterocycles and Carbocycles. *Acc. Chem. Res.* **2019**, *52*, 425−436. For selected reports, see (g) De Sarkar, S.; Studer, A. NHC-Catalyzed Michael Addition to α,β-Unsaturated Aldehydes by Redox Activation. *Angew. Chem., Int. Ed.* **2010**, *49*, 9266−9269. (h) Ryan, S. J.; Candish, L.; Lupton, D. W. N-Heterocyclic Carbene-Catalyzed [4 + 2] Cycloaddition/ Decarboxylation of Silyl Dienol Ethers with α,β-Unsaturated Acid Fluorides. *J. Am. Chem. Soc.* **2011**, *133*, 4694−4697. (i) Anwar, M.; Yang, S.; Xu, W.; Liu, J.; Perveen, S.; Kong, X.; Zehra, S. T.; Fang, X. Carbene-Catalyzed Asymmetric Friedel-Crafts Alkylation-Annulation Sequence and Rapid Synthesis of Indole-Fused Polycyclic Alkaloids. *Commun. Chem.* **2019**, *2*, 85.

(11) See the Supporting Information for more details.

(12) (a) Snyder, S. A.; Breazzano, S. P.; Ross, A. G.; Lin, Y.; Zografos, A. L. Total Synthesis of Diverse Carbogenic Complexity within the Resveratrol Class from a Common Building Block. *J. Am. Chem. Soc.* **2009**, *131*, 1753−1765. (b) Kurzawa, T.; Harms, K.; Koert, U. Stereoselective Synthesis of the Benzodihydropentalene Core of the Fijiolides. *Org. Lett.* **2018**, *20*, 1388−1391.

https://doi.org/10.1021/acs.orglett.1c00870
Org. Lett. 2021, 23, 3403−3408