OL Organic Letters

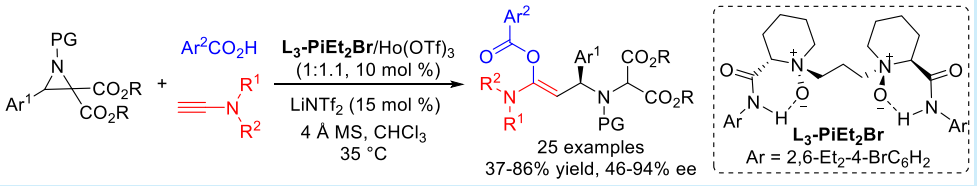
pubs.acs.org/OrgLett Letter

Catalytic Asymmetric Hydroacyloxylation/Ring-Opening Reaction of Ynamides, Acids, and Aziridines

Xiangqiang Li, Hongkun Zeng, Lili Lin,* and Xiaoming Feng*

Cite This: *Org. Lett.* 2021, 23, 2954–2958 Read Online

ACCESS | Metrics & More | Article Recommendations | Supporting Information



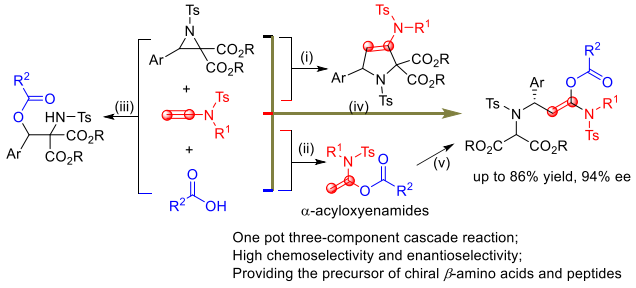
ABSTRACT: A highly enantioselective three-component reaction of ynamides with carboxylic acids and 2,2′-diester aziridines has been realized by using a chiral *N*,*N*′-dioxide/Ho(OTf)$_3$ complex as a Lewis acid catalyst. The process includes the formation of an *α*-acyloxyenamide intermediate through the addition of carboxylic acids to ynamides and the following enantioselective nucleophilic addition to *in-situ*-generated azomethine ylides induced by the chiral catalyst. A range of amino acyloxyenamides are delivered in moderate to good yields with good ee values. In addition, a possible catalytic cycle with a transition model is proposed to elucidate the reaction mechanism.

Downloaded via BUTLER UNIV on May 15, 2021 at 01:51:44 (UTC).
See https://pubs.acs.org/sharingguidelines for options on how to legitimately share published articles.

Multicomponent reactions are attractive for their rapid generation of molecules with broad chemical diversity and molecular complexity from three or more materials in a highly efficient, economic, and environmentally friendly one-pot manner.[1] One difficulty that lies in the catalytic asymmetric multicomponent one-pot reactions is the competitive interaction among reactants as well as the catalyst.[2] Because of the activation by the nitrogen atom, the C≡C bond in the ynamides is strongly polarized and shows a good differentiation between the two carbon atoms.[3,4] Recently, Cui's group reported BF_3-promoted multicomponent reactions (MCRs) of ynamides, organic acids with aldehydes,[5a] imines,[5b] and *ortho*-quinone methides,[5c] giving racemic *β*-acyloxyamide, *β*-amino amide, and diarylpropanamide products. These MCRs relied on acyloxyenamide intermediates derived from ynamides and carboxylic acids (Scheme 1, path ii). Our group realized the first catalytic asymmetric three-component cascade reaction of ynamides and *ortho*-hydroxybenzyl alcohols by developing a chiral *N*,*N*′-dioxide/Sc(III) complex catalytic system.[6]

On the contrary, aziridines are widely used synthetic precursors for synthesizing chiral nitrogenous compounds.[7] Because 2,2′-diester (D-A type) aziridines can undergo C−C bond cleavage to generate azomethine ylides[8] in the presence of a Lewis acid under mild conditions,[9] we assessed that 2,2′-diester aziridines could also be employed as an electrophile to capture the acyloxyenamide intermediates formed by the hydroacyloxylation of ynamides with carboxylic acids (Scheme 1, paths ii and v). The possible challenge arises from the high reactivity of azomethine ylides because they might be readily hydrolyzed in the presence of carboxylic acids and engaged in a two-component reaction with ynamides or carboxylic acids (Scheme 1, paths i and iii). Although difficulties might exist, the resulting chiral amino acyloxyenamides are multifunctional and have a potential use in drug syntheses.[10] Herein we developed a chiral *N*,*N*′-dioxide/Ho(OTf)$_3$ complex catalytic system for the asymmetric three-component hydroacyloxylation/ring opening of ynesulfonamides, carboxylic acids, and 2,2′-diester aziridines, generating chiral amino acyloxyenamides in one pot (Scheme 1, path iv).[11]

Scheme 1. Three-Component Reactions of Ynamides, Aziridines, and Acids



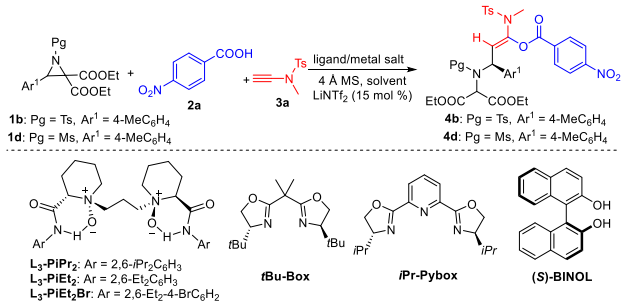
Received: February 22, 2021
Published: March 26, 2021

ACS Publications © 2021 American Chemical Society

https://doi.org/10.1021/acs.orglett.1c00631
Org. Lett. 2021, 23, 2954–2958

Initially, the 2,2′-diester aziridine **1b**, *para*-nitrobenzoic acid **2a**, and *N*-Ts ynamide **3a** were employed to explore the reaction conditions (Table 1). The **L$_3$-PiPr$_3$**/Sc(III)/LiNTf$_2$ catalyst,

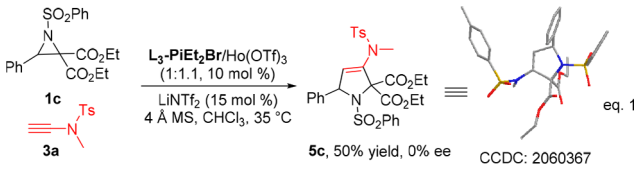
Table 1. Optimization of the Reaction Conditions[a]



entry	meal salt	ligand	solvent	yield (%)[b]	ee (%)[c]
1	Sc(OTf)$_3$	**L$_3$-PiPr$_2$**	toluene	trace	
2	La(OTf)$_3$	**L$_3$-PiPr$_2$**	toluene	11	53
3	Ho(OTf)$_3$	**L$_3$-PiPr$_2$**	toluene	28	57
4	Ho(OTf)$_3$	**L$_3$-PiEt$_2$**	toluene	13	74
5	Ho(OTf)$_3$	**L$_3$-PiEt$_2$Br**	toluene	28	82
6	Ho(OTf)$_3$	**L$_3$-PiEt$_2$Br**	CHCl$_3$	34	90
7[d]	Ho(OTf)$_3$	**L$_3$-PiEt$_2$Br**	CHCl$_3$	51	95
8[e]	Ho(OTf)$_3$	**L$_3$-PiEt$_2$Br**	CHCl$_3$	74	86
9[e,f]	Ho(OTf)$_3$	**L$_3$-PiEt$_2$Br**	CHCl$_3$	86	87
10[e,f]	Ho(OTf)$_3$	***t*Bu-Box**	CHCl$_3$	28	0
11[e,f]	Ho(OTf)$_3$	***i*Pr-Pybox**	CHCl$_3$	15	0
12[e,f]	Ho(OTf)$_3$	**(*S*)-BINOL**	CHCl$_3$	25	0

[a]Unless otherwise noted, all reactions were carried out with ligand/metal salt/LiNTf$_2$ (1:1:1.5, 10 mol %), **1b** (0.10 mmol), **2a** (1.0 equiv), **3a** (1.0 equiv), and 4 Å molecule sieve (50 mg) in solvent (1.0 mL) under a N$_2$ atmosphere at 35 °C for 24 h. [b]Isolated yield. [c]Determined by chiral HPLC analysis. [d]**1b** (1.5 equiv), 4 Å molecule sieves (130 mg), and CHCl$_3$ (2.0 mL) were used. [e]**1d** (1.5 equiv), 4 Å molecule sieves (130 mg), and CHCl$_3$ (2.0 mL) were used. [f]Ligand/metal salt 1:1.1.

which was efficient in the three-component reaction of *ortho*-hydroxybenzyl alcohols with ynamides and carboxylic acid,[6] is inoperative in this reaction (entry 1). Next, various metal salts were screened by complexing with **L$_3$-PiPr$_2$** (entries 2 and 3). The rare-earth metal complex of Ho(OTf)$_3$ could provide the desired product **4b** in 28% yield with 57% ee (entry 3). The low yield was caused by the hydrolysis of aziridine **1b** and the generation of the byproduct 3-pyrroline **5**, which was produced by the [3 + 2] cycloaddition of aziridine **1b** and ynamide **3a** (Scheme 1, path i and eq 1). Then, an examination of the steric

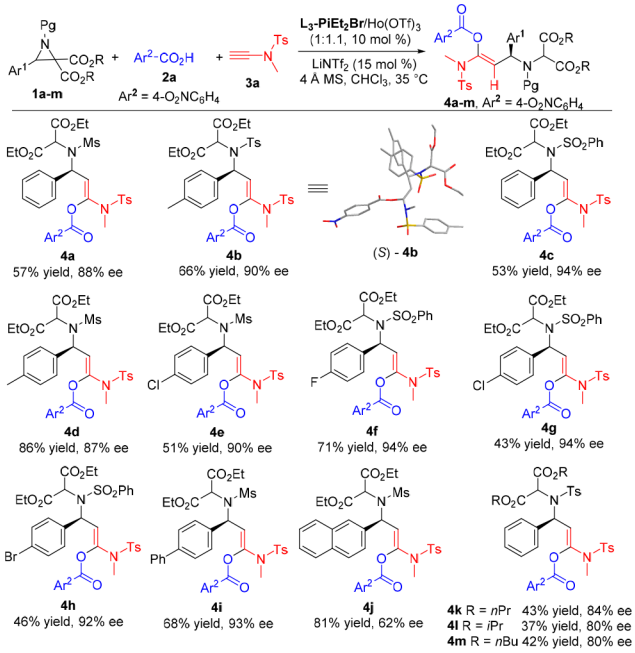


hindrance of the ligands was conducted, and a significant influence on the enantioselectivity was exhibited. **L$_3$-PiEt$_2$** with a decreased steric hindrance improved the ee value to 74%, but the yield decreased (Table 1, entry 4). **L$_3$-PiEt$_2$Br** with a bromo atom at the para position of phenyl ring further improved the ee to 82% ee with the yield remaining low (entry 5). When the reaction was carried out in CHCl$_3$, the yield could be increased to 34%, and the enantioselectivity increased to 90% ee (entry 6).

To reduce the impact of the erosion of diester aziridine under Lewis acidic conditions, the amount of **1b** was increased to 1.5 equiv, and the amount of 4 Å molecular sieve, which can slow down the hydrolysis of azomethine ylides, was increased from 50 to 130 mg, and thus the desired **4b** was obtained in 51% yield with 95% ee (entry 7). Moreover, the yield could be increased to 74% with the ee value reduced to 86% (entry 8) when *N*-methanesulfonyl protecting diester aziridine **1d** was used as the substrate, probably because the *N*-methanesulfonyl protecting group enhances the stability of the azomethine ylides formed *in situ* from 2,2′-diester aziridines. It was surprising that a small excessive amount of metal salt (**L$_3$-PiEt$_2$Br**/Ho(OTf)$_3$ = 1/1.1) could further increase the reactivity with maintained enantioselectivity (entry 9, 86% yield, 87% ee). Under the current reaction conditions, the two-component [3 + 2] cycloaddition product **5d** could be isolated with ∼10% yield. However, when 2,2′-diester aziridine **1c** and ynamide **3a** were mixed under optimized conditions, [3 + 2] cycloaddition occurred and delivered the tetra-substituted 3-pyrroline **5c** in 50% yield without enantioselectivity (eq 1). In addition, we surveyed other ligands. Superior Box and BINOL did not give any enantioselectivity (entries 10−12).

Next, we turned our attention to the substrate generality under optimal reaction conditions. First, diester aziridines **1a**−**1m** were investigated. As shown in Scheme 2, **1a**−**1d** with an *N*-

Scheme 2. Substrate Scope of 2,2′-Diester Aziridines[a]



[a]All reactions were carried out with **L$_3$-PiEt$_2$Br**/Ho(OTf)$_3$/LiNTf$_2$ (1:1.1:1.5, 10 mol %), **1** (1.5 equiv), **2a** (0.10 mmol), **3a** (1.0 equiv), and 4 Å molecule sieve (130 mg) in CHCl$_3$ (2.0 mL) under a N$_2$ atmosphere at 35 °C for 24 h.

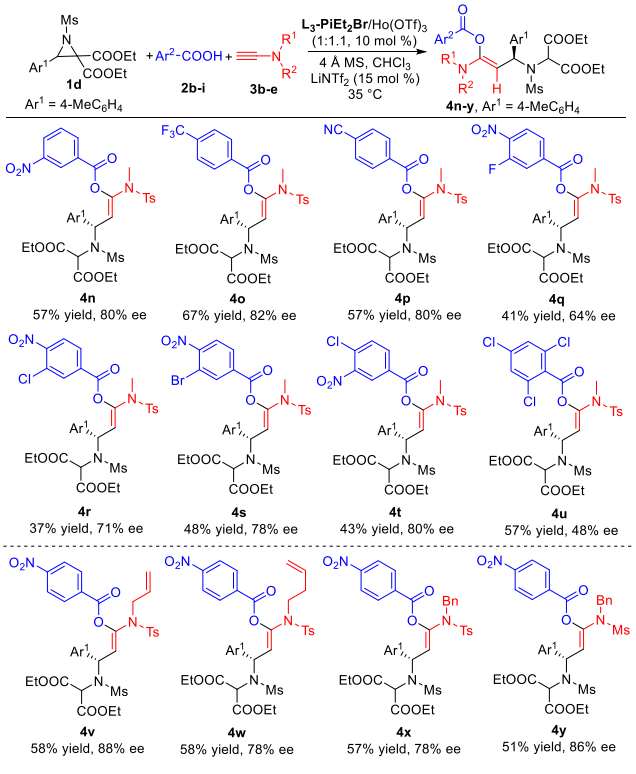
methylsulfonyl protecting group or *N*-phenylsulfonyl protecting group could afford the corresponding products **4a**−**4d** in moderate yields with good ee values (53−86% yield, 87−94% ee). **1d**−**1i** bearing different substituent groups, such as Me−, F−, Cl−, Br−, and phenyl−, on the para position of the Ar^1 ring could be transformed to the corresponding products **4d**−**4i** in moderate to good yields with good ee values (43−86% yield, 87−94% ee). When 2-naphthyl-substituted diester aziridine **1j**

https://doi.org/10.1021/acs.orglett.1c00631
Org. Lett. 2021, 23, 2954−2958

was applied, the product **4j** could be obtained in 81% yield with 62% ee. Moreover, aziridines **1k**−**1m** with dipropyl, diisopropyl, or dibutyl esters were also tolerated in this three-component process and furnished the corresponding products **4k**−**4m** in moderate yields with good ee values. Aziridines with strong electron-donating groups in Ar^1 were not suitable. The reaction mixtures were complex, and only trace amounts of the desired products could be detected. The reason might be that the corresponding azomethine ylides are unstable. The absolute configuration of the product **4b** was determined to be (*S*) by X-ray single-crystal analysis. To show the synthetic utility of the methodology, a gram-scale synthesis of **4b** was performed. Under the optimized reaction conditions, **1b** (3.75 mmol), **2a** (2.50 mmol), and **3a** (2.50 mmol) reacted smoothly, affording 1.22 g of the product **4b** in 60% yield with 90% ee. (See the details in the Supporting Information (SI).)

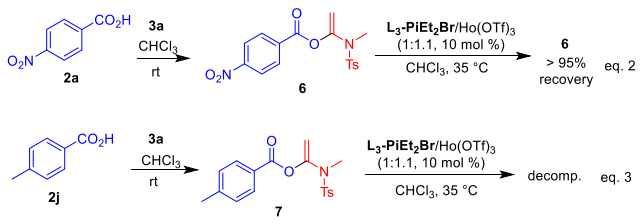
Subsequently, the carboxylic acids **2** and ynamides **3** were varied. As shown in Scheme 3, carboxylic acids **2b**−**2d** with

Scheme 3. Substrate Scope of Carboxylic Acids and Ynamides.[a]

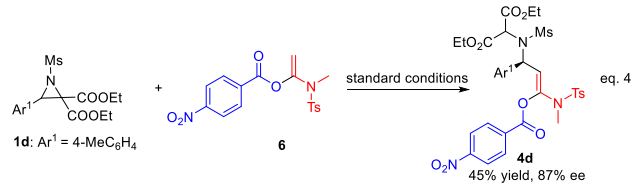


[a]All reactions were carried out with L_3-**PiEt$_2$Br**/Ho(OTf)$_3$/LiNTf$_2$ (1:1.1:1.5, 10 mol %), 4 Å molecule sieve (130 mg), **1d** (1.5 equiv), **2** (0.10 mmol), and **3** (1.0 equiv) in $CHCl_3$ (2.0 mL) under a N_2 atmosphere at 35 °C for 24 h.

O_2N, F_3C, or NC groups at the meta or para position of the phenyl ring furnished this three-component reaction well and provided the corresponding products **4n**−**4p** in 57−67% yield with 80−82% ee. Next, a range of nitrobenzoic acids **2e**−**2h** substituted by halogen atoms at the three- or four-position of the phenyl ring were investigated, and the corresponding products **4q**−**4t** were obtained in 37−48% yields with 64−80% ee. 2,4,6-Trichlorobenzoic acid **2i** produced product **4u** in 57% yield with 48% ee. Benzoic acids with electron-donating groups caused the reaction mixture to be complex, which might be because the *α*-acyloxyenamide intermediates are unstable (eq 2 vs eq 3). The stability of intermediate **6** under L_3-**PiEt$_2$Br**/Ho(OTf)$_3$



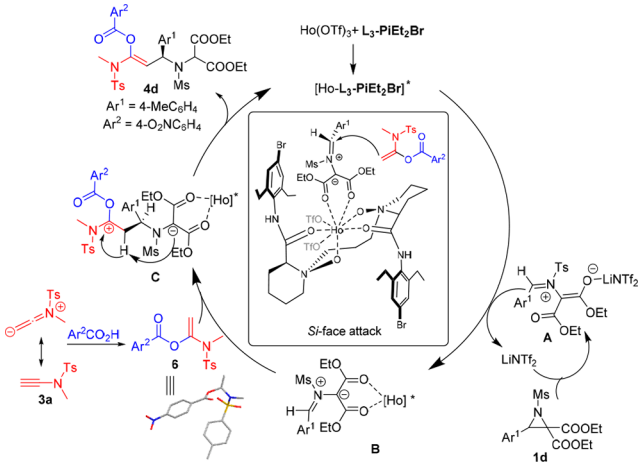
conditions was conducted in $CHCl_3$, and nearly no decomposition occurred. Nevertheless, under the same conditions, the electron-donating-group-substituted enamide **7** partially decomposed. To get insight into the more mechanistic implications, the reaction between enamide **6** and 2,2′-diester aziridine **1d** was carried out under the optimal conditions (eq 4), and the product **4d** was delivered in 45% yield with 87% ee, which means that the acyloxyenamide intermediate should be the actual intermediate.



Different ynamides were also surveyed under the optimized conditions. Ynamides bearing different *N*-alkyl groups (such as allyl, 3-butenyl, or benzyl groups) performed well under the optimized reaction conditions, delivering the corresponding products **4v**−**4x** in moderate yields with good ee values (57−58% yields, 78−88% ee). Ynamide **3e** with *N*-methanesulfonyl group was also suitable, and the desired product **4y** was obtained in 51% yield with 86% ee. The absolute configurations of the products **4a**−**4y** were also determined to be (*S*) by comparing the circular dichroism spectra with that of **4b**. (See the details in the SI).

On the basis of the experimental phenomena, the determination of the absolute configuration of the products, and our previous works,[6] a plausible catalytic cycle with a transition-state model is proposed. As shown in Scheme 4, the tetradentate L_3-**PiEt$_2$Br** coordinates to Ho(OTf)$_3$, forming the

Scheme 4. Proposed Reaction Mechanism



https://doi.org/10.1021/acs.orglett.1c00631
Org. Lett. 2021, 23, 2954−2958

L_3-**PiEt$_2$Br**/Ho(III) complex. Meanwhile, the azomethine ylide intermediate **A** is generated through the cleavage of the carbon−carbon bond in aziridines **1d** under the assistance of $LiNTf_2$. Because of the strong bidentate coordination of two ester groups to the metal center, the chiral L_3-**PiEt$_2$Br**/Ho(III) complex can readily catch the azomethine ylide to form intermediate **B**. The coordination is also supported by the high-resolution electrospray ionization mass spectrometry (ESI-HRMS) analysis of the mixture of L_3-**PiEt$_2$Br**, $Ho(OTf)_3$, and **1d**, as the characteristic signal of $[L_3\text{-}PiEt_2Br\text{-}Ho^{3+}\text{-}2(OTf^-)\text{-}1d]^+$ m/z = 1568.1588 (m/z calcd 1568.1606) was found. The *Re* face of azomethine ylide intermediate **B** is strongly shielded by the neighboring 2,6-diethyl-4-bromo group of the ligand L_3-**PiEt$_2$Br**. As a result, the *N*-Ts iminium carbon of intermediate **B** is attacked by the acyloxyenamide **6** from **B**'s *Si* face, delivering the intermediate **C**. Finally, the intermediate **C** undergoes a 1,4-proton shift and furnishes the desired product (*S*)-**4d**.

In summary, the catalytic asymmetric three-component cascade hydroacyloxylation/ring-opening reaction of aziridines with ynamides and carboxylic acids has been realized by using a chiral *N*,*N*′-dioxide/$Ho(OTf)_3$ complex as the chiral Lewis acid catalyst. This protocol provides a facile and efficient access to chiral amino acyloxyenamides under mild reaction conditions. Moreover, a plausible catalytic cycle has been proposed to explain the reaction mechanism. Further development of asymmetric multicomponent reactions (AMCRs) is ongoing in our group.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.orglett.1c00631.

Experimental procedures, full spectroscopic data for all new compounds, and copies of ^1H, $^{13}C\{^1H\}$, and $^{19}F\{^1H\}$ NMR and HPLC spectra (PDF)

Accession Codes

CCDC 2021534 and 2060367 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

Lili Lin − *Key Laboratory of Green Chemistry & Technology, Ministry of Education, College of Chemistry, Sichuan University, Chengdu 610064, China*; orcid.org/0000-0001-8723-6793; Email: lililin@scu.edu.cn

Xiaoming Feng − *Key Laboratory of Green Chemistry & Technology, Ministry of Education, College of Chemistry, Sichuan University, Chengdu 610064, China*; orcid.org/0000-0003-4507-0478; Email: xmfeng@scu.edu.cn

Authors

Xiangqiang Li − *Key Laboratory of Green Chemistry & Technology, Ministry of Education, College of Chemistry, Sichuan University, Chengdu 610064, China*

Hongkun Zeng − *Key Laboratory of Green Chemistry & Technology, Ministry of Education, College of Chemistry, Sichuan University, Chengdu 610064, China*

Complete contact information is available at: https://pubs.acs.org/10.1021/acs.orglett.1c00631

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We appreciate the financial support from the National Natural Science Foundation of China (nos. 21890723 and 21871188).

■ REFERENCES

(1) For selected reviews of MCRs, see: (a) Dömling, A. Recent Developments in Isocyanide Based Multicomponent Reactions in Applied Chemistry. *Chem. Rev.* **2006**, *106*, 17−89. (b) Dömling, A.; Wang, W.; Wang, K. Chemistry and Biology of Multicomponent Reactions. *Chem. Rev.* **2012**, *112*, 3083−3135. (c) Garbarino, S.; Ravelli, D.; Protti, S.; Basso, A. Photoinduced Multicomponent Reactions. *Angew. Chem., Int. Ed.* **2016**, *55*, 15476−15484. (d) Ghasemzadeh, M. A.; Mirhosseini-Eshkevari, B.; Tavakoli, M.; Zamani, F. Metal−organic Frameworks: Advanced Tools for Multicomponent Reactions. *Green Chem.* **2020**, *22*, 7265−7300.

(2) For selected reviews of AMCRs, see: (a) Ramón, D. J.; Yus, M. Asymmetric Multicomponent Reactions (AMCRs): The New Frontier. *Angew. Chem., Int. Ed.* **2005**, *44*, 1602−1634. (b) de Graaff, C.; Ruijter, E.; Orru, R. V. A. Recent Developments in Asymmetric Multicomponent Reactions. *Chem. Soc. Rev.* **2012**, *41*, 3969−4009. (c) Wang, Q.; Wang, D.-X.; Wang, M.-X.; Zhu, J. Still Unconquered: Enantioselective Passerini and Ugi Multicomponent Reactions. *Acc. Chem. Res.* **2018**, *51*, 1290−1300. (d) Nunes, P. S. G.; Vidal, H. D. A.; Corrêa, A. G. Recent Advances in Catalytic Enantioselective Multicomponent Reactions. *Org. Biomol. Chem.* **2020**, *18*, 7751−7773. (e) Parvin, T.; Yadav, R.; Choudhury, L. H. Recent Applications of Thiourea-Based Organocatalysts in Asymmetric Multicomponent Reactions (AMCRs). *Org. Biomol. Chem.* **2020**, *18*, 5513−5532.

(3) For selected reviews of ynamides, see: (a) Zificsak, C. A.; Mulder, J. A.; Hsung, R. P.; Rameshkumar, C.; Wei, L.-L. Recent Advances in the Chemistry of Ynamines and Ynamides. *Tetrahedron* **2001**, *57*, 7575−7606. (b) Evano, G.; Coste, A.; Jouvin, K. Ynamides: Versatile Tools in Organic Synthesis. *Angew. Chem., Int. Ed.* **2010**, *49*, 2840−2859. (c) Wang, X.-N.; Yeom, H.-S.; Fang, L.-C.; He, S.; Ma, Z.-X.; Kedrowski, B. L.; Hsung, R. P. Ynamides in Ring Forming Transformations. *Acc. Chem. Res.* **2014**, *47*, 560−578. (d) Hong, F.-L.; Ye, L.-W. Transition Metal-Catalyzed Tandem Reactions of Ynamides for Divergent *N*-Heterocycle Synthesis. *Acc. Chem. Res.* **2020**, *53*, 2003−2019. (e) Chen, Y.-B.; Qian, P.-C.; Ye, L.-W. Brønsted Acid-Mediated Reactions of Ynamides. *Chem. Soc. Rev.* **2020**, *49*, 8897−8909. (f) Lynch, C. C.; Sripada, A.; Wolf, C. Asymmetric Synthesis with Ynamides: Unique Reaction Control, Chemical Diversity and Applications. *Chem. Soc. Rev.* **2020**, *49*, 8543−8583.

(4) For selected examples, see: (a) Zhang, Y.; Hsung, R. P.; Zhang, X.; Huang, J.; Slafer, B. W.; Davis, A. Brønsted Acid-Catalyzed Highly Stereoselective Arene-Ynamide Cyclizations. A Novel Keteniminium Pictet-Spengler Cyclization in Total Syntheses of (±)-Desbromoarborescidines A and C. *Org. Lett.* **2005**, *7*, 1047−1050. (b) Kim, Y.; Dateer, R. B.; Chang, S. Borane-Catalyzed Selective Hydrosilylation of Internal Ynamides Leading to *β*-Silyl (Z)-Enamides. *Org. Lett.* **2017**, *19*, 190−193. (c) Xue, J.; Gao, E.; Wang, X.-N.; Chang, J. Metal-Free Formal Inverse-Electron-Demand Diels-Alder Reaction of 1,2-Diazines with Ynamides. *Org. Lett.* **2018**, *20*, 6055−6058. (d) Habert, L.; Retailleau, P.; Gillaizeau, I. Rapid Synthesis of 3-Amino Isocoumarin Derivatives from Ynamides. *Org. Biomol. Chem.* **2018**, *16*, 7351−7355. (e) Wang, C.-M.; Qi, L.-J.; Sun, Q.; Zhou, B.; Zhang, Z.-X.; Shi, Z.-F.; Lin, S.-C.; Lu, X.; Gong, L.; Ye, L.-W. Transition-Metal-Free Oxidative Cyclization of *N*-Propargyl Ynamides: Stereospecific Construction of Linear Polycyclic *N*-Heterocycles. *Green Chem.* **2018**, *20*, 3271−3278. (f) Jadhav, P. D.; Lu, X.; Liu, R.-S. Gold-Catalyzed [5 + 2]- and [5 + 1]-Annulations between Ynamides and 1,2-Benzisoxazoles with Ligand-

Controlled Chemoselectivity. *ACS Catal.* **2018**, *8*, 9697−9701. (g) Gao, Y.; Wu, G.; Zhou, Q.; Wang, J. Palladium-Catalyzed Oxygenative Cross-Coupling of Ynamides and Benzyl Bromides by Carbene Migratory Insertion. *Angew. Chem., Int. Ed.* **2018**, *57*, 2716−2750. (h) Prabagar, B.; Mallick, R. K.; Prasad, R.; Gandon, V.; Sahoo, A. K. Umpolung Reactivity of Ynamides: An Unconventional [1,3]-Sulfonyl and [1,5]-Sulfinyl Migration Cascade. *Angew. Chem., Int. Ed.* **2019**, *58*, 2365−2370. (i) Zhou, B.; Tan, T.-D.; Zhu, X.-Q.; Shang, M.; Ye, L.-W. Reversal of Regioselectivity in Ynamide Chemistry. *ACS Catal.* **2019**, *9*, 6393−6406. (j) Zhang, Y.-Q.; Zhu, X.-Q.; Xu, Y.; Bu, H.-Z.; Wang, J.-L.; Zhai, T.-Y.; Zhou, J.-M.; Ye, L.-W. Synthesis of Functionalized 3-Isochromanones via Metal-Free Intramolecular Alkoxylation-Initiated Cascade Cyclization. *Green Chem.* **2019**, *21*, 3023−3028. (k) Wu, H.; Liu, Y.; He, M.; Wen, H.; Cao, W.; Chen, P.; Tang, Y. Preparation of Isoquinazolines via Metal-Free [4 + 2] Cycloaddition of Ynamides with Nitriles. *Org. Biomol. Chem.* **2019**, *17*, 8408−8416. (l) Li, J.-L.; Lin, E.; Han, X.-L.; Li, Q.; Wang, H. Synthesis of α-Fluorinated Imides via Direct Fluorohydroxylation of Ynamides. *Org. Lett.* **2019**, *21*, 4255−4258. (m) Zhou, B.; Zhang, Y.-Q.; Zhang, K.; Yang, M.-Y.; Chen, Y.-B.; Li, Y.; Peng, Q.; Zhu, S.-F.; Zhou, Q.-L.; Ye, L.-W. Stereoselective Synthesis of Medium Lactams Enabled by Metal-Free Hydroalkoxylation/Stereospecific [1,3]-Rearrangement. *Nat. Commun.* **2019**, *10*, 3234−3245. (n) Xu, Y.; Sun, Q.; Tan, T.-D.; Yang, M.-Y.; Yuan, P.; Wu, S.-Q.; Lu, X.; Hong, X.; Ye, L.-W. Organocatalytic Enantioselective Conia-Ene-Type Carbocyclization of Ynamide Cyclohexanones: Regiodivergent Synthesis of Morphans and Normorphans. *Angew. Chem., Int. Ed.* **2019**, *58*, 16252−16259. (o) Moskowitz, M.; Wolf, C. Catalytic Enantioselective Ynamide Additions to Isatins: Concise Access to Oxindole Alkaloids. *Angew. Chem., Int. Ed.* **2019**, *58*, 3402−3406. (p) Thilmany, P.; Evano, G. Efficient and Divergent Synthesis of α-Halogenated Amides and Esters by Double Electrophilic Activation of Ynamides. *Angew. Chem., Int. Ed.* **2020**, *59*, 242−246. (q) Dutta, S.; Yang, S.; Vanjari, R.; Mallick, R. K.; Gandon, V.; Sahoo, A. K. Keteniminium-Driven Umpolung Difunctionalization of Ynamides. *Angew. Chem., Int. Ed.* **2020**, *59*, 10785−10790. (r) Zeng, L.; Lin, Y.; Li, J.; Sajiki, H.; Xie, H.; Cui, S. Skeletal reorganization divergence of *N*-sulfonyl ynamides. *Nat. Commun.* **2020**, *11*, 5639−5649.

(5) (a) Shen, Y.; Huang, B.; Zeng, L.; Cui, S. Single Reactant Replacement Approach of Passerini Reaction: One-Pot Synthesis of β-Acyloxyamides and Phthalides. *Org. Lett.* **2017**, *19*, 4616−4619. (b) Huang, B.; Zeng, L.; Shen, Y.; Cui, S. One-Pot Multicomponent Synthesis of β-Amino Amides. *Angew. Chem., Int. Ed.* **2017**, *56*, 4565−4568. (c) Chen, R.; Liu, Y.; Cui, S. 1,4-Conjugate addition/Esterification of *ortho*-Quinone Methides in a Multicomponent Reaction. *Chem. Commun.* **2018**, *54*, 11753−11756.

(6) Li, X. Q.; Jiang, M. Y.; Zhan, T. Y.; Cao, W. D.; Feng, X. M. Catalytic Asymmetric Three-component Hydroacyloxylation/ 1,4-Conjugate Addition of Ynamides. *Chem. - Asian J.* **2020**, *15*, 1953−1956.

(7) For selected reviews, see: (a) Singh, G. S.; D'hooghe, M.; De Kimpe, N. Synthesis and Reactivity of C-Heteroatom-Substituted Aziridines. *Chem. Rev.* **2007**, *107*, 2080−2135. (b) Lu, P. Recent Developments in Regioselective Ring Opening of Aziridines. *Tetrahedron* **2010**, *66*, 2549−2560. (c) Ohno, H. Synthesis and Applications of Vinylaziridines and Ethynylaziridines. *Chem. Rev.* **2014**, *114*, 7784−7814. (d) Huang, C.-Y.; Doyle, A. G. The Chemistry of Transition Metals with Three-Membered Ring Heterocycles. *Chem. Rev.* **2014**, *114*, 8153−8198. (e) Feng, J.-J.; Zhang, J. Synthesis of Unsaturated *N*-Heterocycles by Cycloadditions of Aziridines and Alkynes. *ACS Catal.* **2016**, *6*, 6651−6661.

(8) For selected reviews, see: (a) Dauban, P.; Malik, G. A Masked 1,3-Dipole Revealed from Aziridines. *Angew. Chem., Int. Ed.* **2009**, *48*, 9026−9029. (b) Tang, S.; Zhang, X.; Sun, J.; Niu, D.; Chruma, J. J. 2-Azaallyl Anions, 2-Azaallyl Cations, 2-Azaallyl Radicals, and Azomethine Ylides. *Chem. Rev.* **2018**, *118*, 10393−10457.

(9) For selected examples, see: (a) Pohlhaus, P. D.; Bowman, R. K.; Johnson, J. S. Lewis Acid-Promoted Carbon-Carbon Bond Cleavage of Aziridines: Divergent Cycloaddition Pathways of the Derived Ylides. *J. Am. Chem. Soc.* **2004**, *126*, 2294−2295. (b) Wu, X.; Li, L.; Zhang, J. Nickel(II)-Catalyzed Diastereoselective [3 + 2] Cycloaddition of *N*-Tosyl-Aziridines and Aldehydes via Selective Carbon-Carbon Bond Cleavage. *Chem. Commun.* **2011**, *47*, 7824−7826. (c) Li, L.; Zhang, J. Lewis Acid-Catalyzed [3 + 2] Cycloaddition of Alkynes with *N*-Tosyl-aziridines via Carbon-Carbon Bond Cleavage: Synthesis of Highly Substituted 3-Pyrrolines. *Org. Lett.* **2011**, *13*, 5940−5943. (d) Liu, H.; Zheng, C.; You, S.-L. $Fe(OTf)_3$ Catalyzed Annulation of 2,3-Disubstituted Indoles with Aziridines. *Chin. J. Chem.* **2014**, *32*, 709−714. (e) Ghosh, A.; Pandey, A. K.; Banerjee, P. Lewis Acid Catalyzed Annulation of Donor-Acceptor Cyclopropane and *N*-Tosylaziridinedicarboxylate: One-Step Synthesis of Functionalized 2*H*-Furo [2,3-*c*] pyrroles. *J. Org. Chem.* **2015**, *80*, 7235−7242. (f) Soeta, T.; Miyamoto, Y.; Fujinami, S.; Ukaji, Y. The Lewis Acid-Catalyzed [3 + 1+1] Cycloaddition of Azomethine Ylides with Isocyanides. *Tetrahedron* **2014**, *70*, 6623−6629. (g) Craig, R. A., II; O'Connor, N. R.; Goldberg, A. F. G.; Stoltz, B. M. Stereoselective Lewis Acid Mediated (3 + 2) Cycloadditions of *N*-H- and *N*-Sulfonylaziridines with Heterocumulenes. *Chem. - Eur. J.* **2014**, *20*, 4806−4813. (h) Wang, B.; Liang, M.; Tang, J.; Deng, Y.; Zhao, J.; Sun, H.; Tung, C.-H.; Jia, J.; Xu, Z. Gold/Lewis Acid Catalyzed Cycloisomerization/Diastereoselective [3 + 2] Cycloaddition Cascade: Synthesis of Diverse Nitrogen-Containing Spiro Heterocycles. *Org. Lett.* **2016**, *18*, 4614−4617. (i) Liao, Y. T.; Liu, X. H.; Zhang, Y.; Xu, Y. L.; Xia, Y.; Lin, L. L.; Feng, X. M. Asymmetric [3 + 2] CyCloaddition of Donor-Acceptor Aziridines with Aldehydes via Carbon-Carbon Bond Cleavage. *Chem. Sci.* **2016**, *7*, 3775−3779. (j) Li, L.; Wu, X.; Zhang, J. Lewis Acid-Catalyzed Formal [3 + 2] Cycloadditions of *N*-Tosyl Aziridines with Electron-Rich Alkenes via Selective Carbon-Carbon Bond Cleavage. *Chem. Commun.* **2011**, *47*, 5049−5051. (k) Liao, Y. T.; Zhou, B. X.; Xia, Y.; Liu, X. H.; Lin, L. L.; Feng, X. M. Asymmetric [3 + 2] Cycloaddition of 2,2′-Diester Aziridines To Synthesize Pyrrolidine Derivatives. *ACS Catal.* **2017**, *7*, 3934−3939. (l) Xu, Y. L.; Chang, F. Z.; Cao, W. D.; Liu, X. H.; Feng, X. M. Catalytic Asymmetric Chemodivergent C2 Alkylation and [3 + 2]-Cycloaddition of 3-Methylindoles with Aziridines. *ACS Catal.* **2018**, *8*, 10261−10266.

(10) For selected reports on the synthesis of chiral β-amino acids and chiral peptides, see: (a) Ikemoto, N.; Tellers, D. M.; Dreher, S. D.; Liu, J.; Huang, A.; Rivera, N. R.; Njolito, E.; Hsiao, Y.; McWilliams, J. C.; Williams, J. M.; Armstrong, J. D.; Sun, Y.; Mathre, D. J.; Grabowski, E. J. J.; Tillyer, R. D. Highly Diastereoselective Heterogeneously Catalyzed Hydrogenation of Enamines for the Synthesis of Chiral β-Amino Acid Derivatives. *J. Am. Chem. Soc.* **2004**, *126*, 3048−3049. (b) Gouge, V.; Jubault, P.; Quirion, J.-C. Synthesis of Difluorinated Pseudo Peptides Using Chiral α,α-Difluoro-β-Amino Acids in the Ugi Reaction. *Tetrahedron Lett.* **2004**, *45*, 773−776. (c) Nyerges, M.; Bendell, D.; Arany, A.; Hibbs, D. E.; Coles, S. J.; Hursthouse, M. B.; Groundwater, P. W.; Meth-Cohn, O. Silver Acetate-Catalysed Asymmetric 1,3-Dipolar Cycloadditions of Imines and Chiral Acrylamides. *Tetrahedron* **2005**, *61*, 3745−3753.

(11) For recent reports of *N*,*N*′-dioxides/metal salt complexes, see: (a) Liu, X. H.; Lin, L. L.; Feng, X. M. Chiral *N*,*N*′-Dioxides: New Ligands and Organocatalysts for Catalytic Asymmetric Reactions. *Acc. Chem. Res.* **2011**, *44*, 574−587. (b) Liu, X. H.; Lin, L. L.; Feng, X. M. Chiral *N*,*N*′-Dioxide Ligands: Synthesis, Coordination Chemistry and Asymmetric Catalysis. *Org. Chem. Front.* **2014**, *1*, 298−302. (c) Liu, X. H.; Zheng, H. F.; Xia, Y.; Lin, L. L.; Feng, X. M. Asymmetric Cycloaddition and Cyclization Reactions Catalyzed by Chiral *N*,*N*′-Dioxide-Metal Complexes. *Acc. Chem. Res.* **2017**, *50*, 2621−2631. (d) Liu, X. H.; Dong, S. X.; Lin, L. L.; Feng, X. M. Chiral Amino Acids-Derived Catalysts and Ligands. *Chin. J. Chem.* **2018**, *36*, 791−797.

https://doi.org/10.1021/acs.orglett.1c00631
Org. Lett. 2021, 23, 2954−2958