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Asymmetric Synthesis of α,β-Epoxy-γ-lactams through Tandem Darzens/Hemiaminalization Reaction

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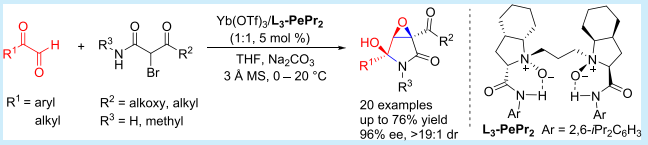
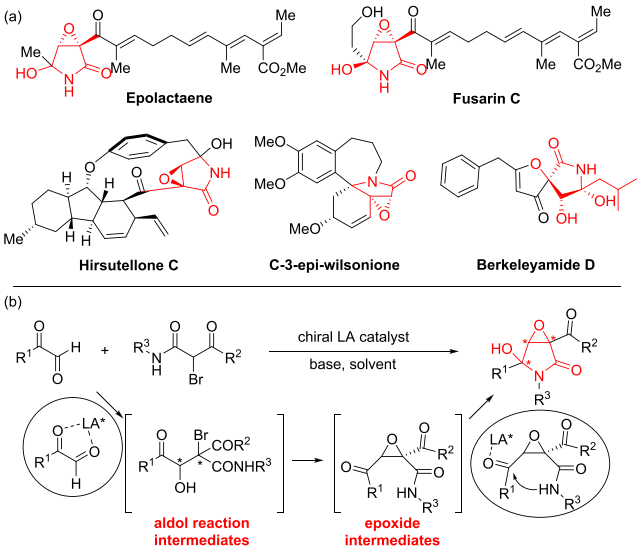
Supporting Information

ABSTRACT: A catalytic asymmetric tandem Darzens/hemiaminalization reaction of glyoxals with α-bromo-β-esteramides or α-bromo-β-ketoamide was accomplished in the presence of a chiral *N,N′*-dioxide/Yb(III) complex. Various chiral α,β-epoxy-γ-lactams were obtained in moderate to good yields with excellent diastereo- and enantioselectivities. The versatility of the transformation is illustrated in the formal synthesis of berkeleyamide D.



α,β-Epoxy-γ-lactams are a highly valuable skeleton that is present in a plethora of biologically active molecules, such as epolctaene,[1] fusarin C,[2] hirsutellone C,[3] and C-3-*epi*-wilsonione[4] (Scheme 1a). They can also serve as attractive building blocks to access more complex molecular architectures, including the synthesis of salinosporamide A,[5] lucilactaene,[6] azaspirene,[7] and berkeleyamide D.[8] The valuable biological activities of these related natural products, as well as a novel 3-acyl-5-hydroxyl-3,4-epoxy-2-pyrrolidinone structure characteristic, have attracted considerable interest from synthesis chemists. The Darzens/hemiaminalization reaction between glyoxals and α-bromo-β-ketoamide provides a straightforward route for the construction of this key moiety,[8,9] which contains three stereogenic centers (Scheme 1b). This method has been used for the short synthesis of (±)-berkeleyamide D; however, the optically enriched enantiomers were obtained by resolution with chiral HPLC.[8a] As asymmetric catalysis is an extremely important method to generate chiral compounds, the development of an efficient asymmetric catalytic version of this Darzens/hemiaminalization reaction is useful but challenging.

Scheme 1. (a) Selected Natural Products Bearing α,β-Epoxy-γ-Lactam Structure; (b) Darzens/Hemiaminalization Reaction for the Construction of Epoxypyrrolidinone Derivatives



Catalytic asymmetric Darzens reaction,[10] which generally employs the base-induced sequence of aldol reaction/intramolecular cyclization, is demonstrated to be one of the powerful approaches for the preparation of chiral epoxy compounds.[11] Both chiral organocatalysis and Lewis acid catalysis have been successfully used in enantioselective Darzens reactions. However, the type of nucleophilic species is limited to α-halo carbonyl compounds, chloroacetonitrile, chloromethylsulfones, or 2-halo-1-indanone. The difficulties related to the target asymmetric tandem Darzens/hemiaminalization include the following: (1) α-bromo-β-ketoamides or α-bromo-β-esteramides are new nucleophiles in the Darzens reaction, and their steric hindrance might hamper the addition and S_N2 cyclization processes; (2) the diastereomeric selection in the aldol reaction is directly related to the following formation of epoxide and lactam due to stereochemistry requirements; (3) there are two ring structures and three stereogenic centers in the final product, including two four-substituted carbon centers; (4) both the base-involved background reaction and a retro-aldol process would erode the enantioselectivity of the reaction.[12]

Our research group has achieved good results in a number of asymmetric catalytic transformations, including the Darzens reaction between phenacyl bromides and *N*-protected isatins,[10h] as well as a diastereodivergent formal cyclo-

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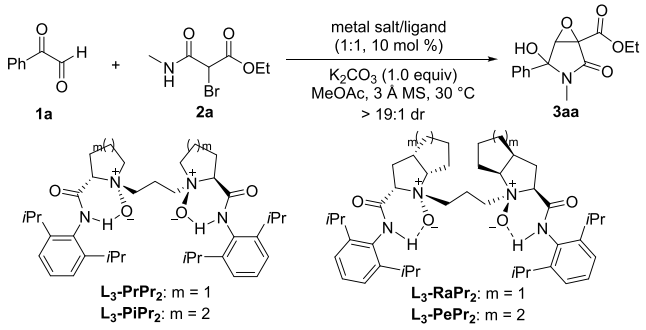
propanation reaction between 3-Cl oxindoles and β,γ-unsaturated-α-ketoesters.[13] These results indicate that chiral Lewis acid catalysts derived from *N,N′*-dioxide and metal salts would enable the titled reaction effectively. The Lewis acid catalyst could activate the carbonyl group of glyoxals[14] and the epoxide intermediate (Scheme 1b), accelerating the initial aldol reaction and the final nucleophilic ring closure, subsequently. The diastereo- and enantioselectivity of the whole process could be controlled by meticulous modification of the chiral *N,N′*-dioxide subunits. Herein, we report a new chiral *N,N′*-dioxide−ytterbium(III) complex[15] catalyzed diastereo- and enantioselective Darzens/hemiaminalization reaction, allowing efficient and direct construction of a number of 3-acyl-5-hydroxyl-3,4-epoxy-2-pyrrolidinone derivatives, including the optically enriched intermediate for the synthesis of berkeleyamide D.

Initially, phenyl glyoxal **1a** and ethyl 2-bromo-3-(methylamino)-3-oxopropanoate **2a** were selected as the model substrates to optimize the reaction conditions (Table 1).

Table 1. Optimization of Reaction Conditions[a]



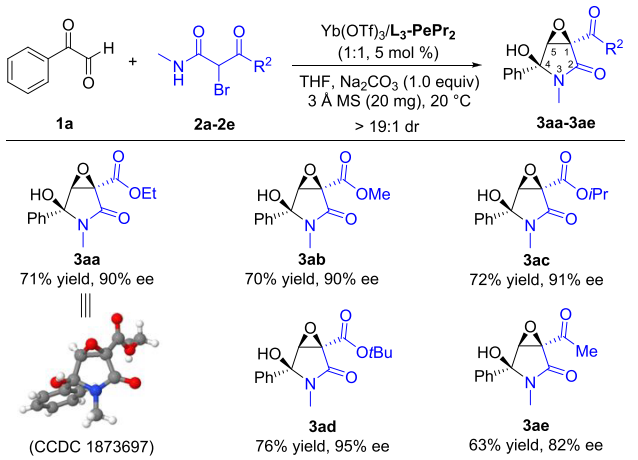
entry	metal salt	ligand	yield (%)[b]	ee (%)[c]
1	$Mg(OTf)_2$	L_3-$RaPr_2$	21	12
2	$Ni(OTf)_2$	L_3-$RaPr_2$	29	10
3	$Sc(OTf)_3$	L_3-$RaPr_2$	30	2
4	$Y(OTf)_3$	L_3-$RaPr_2$	27	68
5	$Yb(OTf)_3$	L_3-$RaPr_2$	57	81
6	$Yb(OTf)_3$	L_3-$PiPr_2$	50	12
7	$Yb(OTf)_3$	L_3-$PrPr_2$	56	26
8	$Yb(OTf)_3$	L_3-$PePr_2$	33	84
9[d]	$Yb(OTf)_3$	L_3-$PePr_2$	65	88
10[d,e]	$Yb(OTf)_3$	L_3-$PePr_2$	64	90
11[d−f]	$Yb(OTf)_3$	L_3-$PePr_2$	71	90
12[d−g]	$Yb(OTf)_3$	L_3-$PePr_2$	71	90

[a]Unless otherwise noted, the reactions were performed with metal salt/ligand (1:1, 10 mol %), **1a** (0.10 mmol), **2a** (0.10 mmol), K_2CO_3 (1.0 equiv), and 3 Å MS (20 mg) in MeOAc (1.0 mL) at 30 °C for 16 h. [b]Isolated yield; >19/1 dr was obtained. [c]Determined by HPLC analysis on a chiral stationary phase. [d]Na_2CO_3 was used instead of K_2CO_3. [e]THF (1.2 mL) was used instead of MeOAc. [f]20 °C for 24 h. [g]5 mol % catalyst loading for 48 h.

Various metal salts coordinated with chiral *N,N′*-dioxide ligand L_3-$RaPr_2$ were evaluated in this reaction (Table 1, entries 1−5). The corresponding α,β-epoxy-γ-lactam **3aa** could be formed smoothly in the presence of K_2CO_3 as the base. It seemed that lanthanide metal salts as $Y(OTf)_3$ and $Yb(OTf)_3$ showed higher enantioselectivity than other commonly used metals salts, including $Mg(OTf)_2$, $Ni(OTf)_2$, and $Sc(OTf)_3$ in terms of enantioselectivity. Especially, the metal salt of $Yb(OTf)_3$ could promote the reaction to give the desired product **3aa** in 57% yield with excellent diastereoselectivity (>19/1) and good enantioselectivity (81% ee) (Table 1, entry 5). Next, the structure of the *N,N′*-dioxide ligands was investigated. It was found that the chiral pool of the ligands greatly affected the enantioselectivity of the reaction. The screening of the chiral backbone of the ligands revealed L-perindopril derived L_3-$PePr_2$ provided higher enantioselectivity (84% ee) than L_3-$PiPr_2$ (12% ee) derived from *S*-pipecolic acid, L_3-$PrPr_2$ (26% ee) derived from L-proline, and L_3-$RaPr_2$ (81% ee) derived from L-ramipril (Table 1, entry 8 vs entries 5−7). The steric hindrance of the aniline subunits of the ligand had a small amount of influence on the enantioselectivity (see Supporting Information for details). When a weaker base as Na_2CO_3 was used instead of K_2CO_3, both the yield and the ee value had an obvious increase (Table 1, entry 8 vs entry 9). In addition, the enantioselectivity was further improved to 90% ee with THF as the solvent (Table 1, entry 10). Lowering the temperature to 20 °C resulted in a slightly higher yield to 71% (Table 1, entry 11). The yield and ee value could be maintained with a lower catalyst loading (5 mol %) albeit with a prolonged time (Table 1, entry 12). Therefore, the optimal reaction conditions were established as **1a** and **2a** (1.0 equiv), $Yb(OTf)_3$/L_3-$PePr_2$ (1:1, 5 mol %), 3 Å MS, and Na_2CO_3 (1.0 equiv) in THF at 20 °C for 48 h.

With the optimized conditions in hand, the substrate generality of the reaction was surveyed. As shown in Scheme 2, α-bromo-β-esteramides **2a**−**2d** bearing different ester

Scheme 2. Substrate Scope of the α-Bromoamides[a]



[a]Unless otherwise noted, the reactions were performed with $Yb(OTf)_3$/L_3-$PePr_2$ (1:1, 5 mol %), **1a** (0.10 mmol), **2** (1.0 equiv), Na_2CO_3 (1.0 equiv), and 3 Å MS (20 mg) in THF (1.2 mL) at 20 °C for 48 h. >19/1 dr.

groups, including methyl, ethyl, isopropyl, and tertbutyl substituents, could react with **1a** smoothly to produce the corresponding products **3aa**−**3ad** in good yields (70−76% yield) with excellent ee values (90−95% ee). Moreover, the α-bromo-β-ketoamide **2e** was also tolerated and transformed into **3ae** in 63% yield with 82% ee. The absolute configuration of the product **3aa** was determined to be (1*R*,4*S*,5*S*) by X-ray crystallography analysis (CCDC 1873697).

Subsequently, we turned our attention to the scope of glyoxals. The electronic properties or steric hindrance of the substituents on the aromatic ring had a small effect on the stereoselectivity of the tandem reaction, and the desired α,β-

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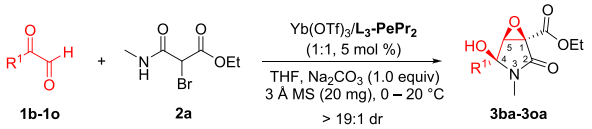
epoxy-γ-lactams **3ba**−**3ma** were obtained with 89−96% ee (Table 2, entries 1−12). The substrate containing electron-

Table 2. Substrate Scope of Glyoxals[a]



entry	R^1	T (°C)	yield (%)[b]	ee (%)[c]
1	3-MeC_6H_4	20	53 (**3ba**)	91
2	3-MeOC_6H_4	20	71 (**3ca**)	92
3	3-ClC_6H_4	10	70 (**3da**)	96
4	3,4-$Cl_2C_6H_3$	20	52 (**3ea**)	93
5	4-MeC_6H_4	20	71 (**3fa**)	92
6	4-FC_6H_4	10	65 (**3ga**)	90
7[d]	4-ClC_6H_4	0	74 (**3ha**)	89
8	4-BrC_6H_4	10	62 (**3ia**)	91
9	4-$CF_3C_6H_4$	10	62 (**3ja**)	94
10	4-PhC_6H_4	20	75 (**3ka**)	93
11	4-tBuC_6H_4	20	74 (**3la**)	90
12[d]	4-$NO_2C_6H_4$	0	61 (**3ma**)	91
13	2-Naphthyl	20	62 (**3na**)	93
14	Cyclohexyl	20	53 (**3oa**)	70

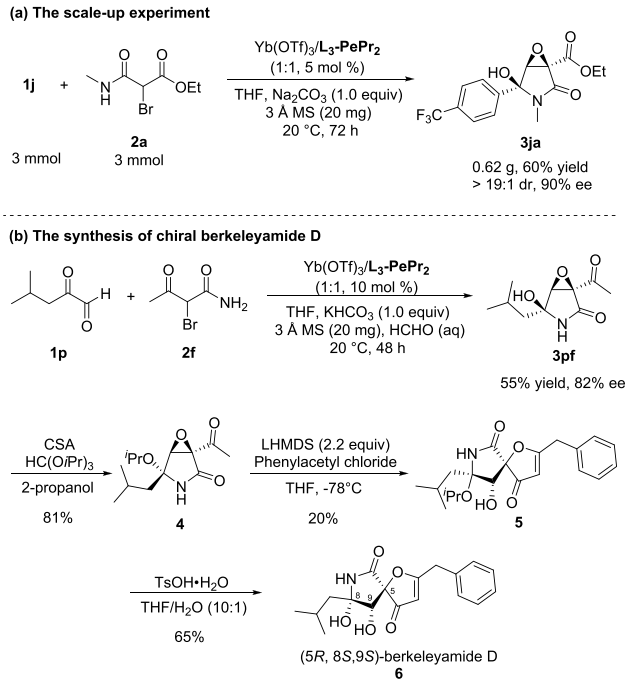
[a]Unless otherwise noted, the reactions were performed with Yb(OTf)$_3$/**L$_3$-PePr$_2$** (1:1, 5 mol %), **1** (1.0 equiv), **2a** (0.10 mmol), Na_2CO_3 (1.0 equiv) and 3 Å MS (20 mg) in THF (1.2 mL) at 20 °C for 48 h. All the products were obtained with >19/1 dr. [b]Isolated yield. [c]Determined by HPLC analysis on a chiral stationary phase. [d]0 °C for 72 h.

withdrawing substituents at the 4-position of the aromatic groups exhibited higher reactivity than that with electron-donating groups (Table 2, entries 6−9, 12 vs entries 5 and 11). In addition, 2-naphthyl- and cyclohexyl-containing glyoaxls were also suitable substrates, giving the products **3na** and **3oa** in 62% yield with 93% ee and 53% yield with 70% ee, respectively (Table 2, entries 13 and 14). It is noteworthy that only one diastereoisomer of the epoxy-pyrrolidinone products was isolated in all cases. The absolute configuration of the products **3ab**−**3ae**, as well as **3ba**−**3na**, were determined to be uniform by comparing the circular-dichroism spectra with that of **3aa**.

To show the practicability of this methodology, a scale-up synthesis of the product **3ja** was carried out. In the presence of 5 mol % of Yb(OTf)$_3$/**L$_3$-PePr$_2$**, glyoxal **1j** (3 mmol) reacted with α-bromo-β-esteramide **2a** (3 mmol) smoothly and delivered **3ja** in 60% yield, >19:1 dr with 90% ee (Scheme 3a). Berkeleyamide D, originally isolated from the extracts of a fungus, shows inhibition of matrix metalloproteinase-3 and caspase-1.[16] Kuramochi and co-workers realized the synthesis of (±)-berkeleyamide D involving the formation of α,β-epoxy-γ-lactam through the Darzens/ring-closure reaction of isobutylglyoxal and α-bromo-β-ketoamide.[8a] After the screening of the reaction conditions in our catalytic system, the reaction between isobutylglyoxal **1p** and α-bromo-β-ketoamide **2f** proceeded smoothly, generating the desired α,β-epoxy-γ-lactam **3pf** in 55% yield with 82% ee. Accordingly, the access to chiral berkeleyamide D is feasible from the chiral **3pf** (Scheme 3b).[8a,17]

In summary, we have presented a highly enantioselective tandem Darzens/ring-closure reaction of glyoxals with α-bromo-β-esteramides or α-bromo-β-ketoamide catalyzed by a chiral *N,N′*-dioxide−Yb(OTf)$_3$ complex. A series of desired α,β-epoxy-γ-lactams were afforded in up to 76% yield with 96% ee and >19:1 dr. In addition, this protocol has been successfully applied to the formal enantioselective synthesis of the biologically active molecule berkeleyamide D.

Scheme 3. Scale-up Experiment and Synthesis of Berkeleyamide D



■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.9b01589.

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

Accession Codes

CCDC 1873697 contains 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.

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) (a) Kuramochi, K.; Nagata, S.; Itaya, H.; Matsubara, Y.; Sunoki, T.; Uchiro, H.; Takao, K.; Kobayashi, S. A Convergent Total Synthesis of Epolactaene: An Application of the Bridgehead Oxiranyl Anion Strategy. *Tetrahedron* **2003**, *59*, 9743. (b) Nagumo, Y.; Kakeya, H.; Shoji, M.; Hayashi, Y.; Dohmae, N.; Oasda, H. Epolactaene Binds Human Hsp60 Cys^{442} Resulting in the Inhibition of Chaperone Activity. *Biochem. J.* **2005**, *387*, 835.

(2) Song, Z.; Cox, R. J.; Lazarus, C. M.; Simpson, T. J. Fusarin C Biosynthesis in *Fusarium moniliforme* and *Fusarium venenatum*. *ChemBioChem* **2004**, *5*, 1196.

(3) Nicolaou, K. C.; Sun, Y.; Sarlah, D.; Zhan, W.; Wu, T. R. Bioinspired Synthesis of Hirsutellones A, B, and C. *Org. Lett.* **2011**, *13*, 5708.

(4) Wang, L.; Su, H.; Yang, S.; Won, S.; Lin, C. New Alkaloids and a Tetraflavonoid from *Cephalotaxus wilsoniana*. *J. Nat. Prod.* **2004**, *67*, 1182.

(5) Ling, T. T.; Potts, B. C.; Macherla, V. R. Concise Formal Synthesis of (−)-Salinosporamide A (Marizomib) Using a Regio- and Stereoselective Epoxidation and Reductive Oxirane Ring-Opening Strategy. *J. Org. Chem.* **2010**, *75*, 3882.

(6) Yamaguchi, J.; Kakeya, H.; Uno, T.; Shoji, M.; Osada, H.; Hayashi, Y. Determination by Asymmetric Total Synthesis of the Absolute Configuration of Lucilactaene, a Cell-Cycle Inhibitor in p53-Transfected Cancer Cells. *Angew. Chem., Int. Ed.* **2005**, *44*, 3110.

(7) Kang, T.; Jo, D.; Han, S. Six-Step Total Synthesis of Azaspirene. *J. Org. Chem.* **2017**, *82*, 9335.

(8) (a) Komori, K.; Taniguchi, T.; Mizutani, S.; Monde, K.; Kuramochi, K.; Tsubaki, K. Short Synthesis of Berkeleyamide D and Determination of the Absolute Configuration by the Vibrational Circular Dichroism Exciton Chirality Method. *Org. Lett.* **2014**, *16*, 1386. (b) Mizutani, S.; Komori, K.; Kai, C.; Kuramochi, K.; Tsubaki, K. The Second Generation Synthesis of (±)-berkeleyamide D. *Tetrahedron* **2016**, *72*, 6640. (c) Kuramochi, K.; Komori, K.; Mizutani, S.; Tsubaki, K. Syntheses of Naturally Occuring Lactams by the Use of Darzens Reaction. *Yuki Gosei Kagaku Kyokaishi* **2018**, *76*, 218.

(9) (a) Hayashi, Y.; Kanayama, J.; Yamaguchi, J.; Shoji, M. Diastereoselective Total Synthesis of Both Enantiomers of Epolactaene. *J. Org. Chem.* **2002**, *67*, 9443. (b) Snider, B. B.; Neubert, B. J. A Novel Biomimetic Route to the 3-Acyl-5-hydroxy-3-pyrrolin-2-one and 3-Acyl-3,4-epoxy-5-hydroxypyrrolidin-2-one Ring Systems. *J. Org. Chem.* **2004**, *69*, 8952. (c) Kuramochi, K.; Mizushina, Y.; Nagata, S.; Sugawara, F.; Sakaguchi, K.; Kobayashi, S. Structure-activity Relationships of Epolactaene Analogs as DNA Polymerases Inhibitors. *Bioorg. Med. Chem.* **2004**, *12*, 1983. (d) Tan, Z.; Negishi, E. Selective Synthesis of Epolactaene Featuring Efficient Construction of Methyl (*Z*)-2-Iodo-2-butenoate and (2*R*,3*S*,4*S*)-2-Trimethylsilyl-2,3-epoxy-4-methyl-γ-butyrolactone. *Org. Lett.* **2006**, *8*, 2783. (e) Rees, D. O.; Bushby, N.; Cox, R. J.; Harding, J. R.; Simpson, T. J.; Willis, C. L. Synthesis of [1,2-$^{13}C_2$, ^{15}N]-L-Homoserine and Its Incorporation by the PKS-NRPS System of *Fusarium moniliforme* into the Mycotoxin Fusarin C. *ChemBioChem* **2007**, *8*, 46. (f) Han, M.; Nam, K.; Hahn, H.; Shin, D. Unexpected Formation of New Bicyclic γ-Lactams by Dimerization of α-Chloroacetoacetanilides. *Tetrahedron Lett.* **2008**, *49*, 5217. (g) Tanaka, K.; Kobayashi, K.; Kogen, H. Total Synthesis of (−)-L-755,807: Establishment of Relative and Absolute Configurations. *Org. Lett.* **2016**, *18*, 1920.

(10) For representative reviews and examples, see: (a) Santos, J.; Retana, A.; Marigorta, E.; Vicario, J.; Palacios, F. Catalytic Asymmetric Darzens and Aza-Darzens Reactions for the Synthesis of Chiral Epoxides and Aziridines. *ChemCatChem* **2018**, *10*, 5092. (b) Arai, S.; Shioiri, T. Catalytiv Asymmetric Darzens Condensation under Phase-Transfer-Catalyzed Conditions. *Tetrahedron Lett.* **1998**, *39*, 2145. (c) Arai, S.; Ishida, T.; Shioiri, T. Asymmetric Synthesis of α,β-Epoxysulfones under Phase-Transfer Catalyzed Darzens Reaction. *Tetrahedron Lett.* **1998**, *39*, 8299. (d) Achard, T.; Belokon, Y.; Ilyin, M.; Moskalenko, M.; North, M.; Pizzato, F. Enantio- and Diastereoselective Darzens Condensation. *Tetrahedron Lett.* **2007**, *48*, 2965. (e) Liu, W. J.; Lv, B. D.; Gong, L. Z. An Asymmetric Catalytic Darzens Reaction between Diazoacetamides and Aldehydes Generates *cis*-Glycidic Amides with High Enantiomeric Purity. *Angew. Chem., Int. Ed.* **2009**, *48*, 6503. (f) Watanabe, S.; Hasebe, R.; Ouchi, J.; Nagasawa, H.; Kataoka, T. Enantioselective Darzens Reaction Using Organoselenide-lithium Hydroxide Complexes. *Tetrahedron Lett.* **2010**, *51*, 5778. (g) Rapi, Z.; Bakó, P.; Keglevich, G.; Szöllösy, Á.; Drahos, L.; Botyánszki, A.; Holczbauer, T. Asymmetric Phase Transfer Darzens Reactions Catalyzed by D-glucose and D-mannose-based Chiral Crown Ethers. *Tetrahedron: Asymmetry* **2012**, *23*, 489. (h) Kuang, Y. L.; Lu, Y.; Tang, Y.; Liu, X. H.; Lin, L. L.; Feng, X. M. Asymmetric Synthesis of Spiro-epoxyoxindoles by the Catalytic Darzens Reaction of Isatins with Phenacyl Bromides. *Org. Lett.* **2014**, *16*, 4244. (i) Zhao, Y.; Xu, P.; Zhang, X.; Chen, S.; Yu, Q.; Wang, Z.; Dai, Z. Synthesis of New Chiral Phase Transfer Catalysts and their Application in the Asymmetric Darzens Reaction. *Austin J. Anal. Pharm. Chem.* **2015**, *2*, 1055.

(11) Rosen, T. *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol. 2, p 409.

(12) Giubellina, N.; Mangelinckx, S.; Törnroos, K. W.; De Kimpe, N. Synthesis of 2-Chloro-2-imidoylaziridines via Aza-Darzens-type Reaction of 3,3-Dichloro-1-azaallylic Anions and *N*-(Arylsulfonyl)-imines. *J. Org. Chem.* **2006**, *71*, 5881.

(13) Kuang, Y. L.; Shen, B.; Dai, L.; Yao, Q.; Liu, X. H.; Lin, L. L.; Feng, X. M. Diastereodivergent Asymmetric Michael-alkylation Reaction Using Chiral *N,N′*-Dioxide/metal Complexes. *Chem. Sci.* **2018**, *9*, 688.

(14) (a) Zheng, K.; Shi, J.; Liu, X. H.; Feng, X. M. Asymmetric Carbonyl-Ene Reaction Catalyzed by Chiral *N,N′*-Dioxide-Nickel(II) Complex: Remarkably Broad Substrate Scope. *J. Am. Chem. Soc.* **2008**, *130*, 15770. (b) Wu, W. B.; Liu, X. H.; Zhang, Y. H.; Ji, J.; Huang, T. Y.; Lin, L. L.; Feng, X. M. Chiral *N,N′*-Dioxide-$FeCl_3$ Complex-catalyzed Asymmetric Intramolecular Cannizzaro Reaction. *Chem. Commun.* **2015**, *51*, 11646. (c) Luo, W. W.; Lin, L. L.; Zhang, Y.; Liu, X. H.; Feng, X. M. Construction of Distant Stereocenters by Enantioselective Desymmetrizing Carbonyl-Ene Reaction. *Org. Lett.* **2017**, *19*, 3374.

(15) For recent reviews on *N,N′*-dioxide/metal 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. (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. (c) Liu, X. H.; Zheng, H. F.; Xia, Y.; Lin, L. L.; Feng, X. M. Asymmetric Cycloaddition and Cyclization Reaction Catalyzed by Chiral *N,N′*-Dioxide-Metal Complexes. *Acc. Chem. Res.* **2017**, *50*, 2621. (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. For selected examples catalyzed by *N,N′*-dioxide/Yb(III), see: (e) Zhang, Y.; Liao, Y. T.; Liu, X. H.; Zhou, Y. H.; Lin, L. L.; Feng, X. M. Catalytic Michael/Ring-Closure Reaction of α,β-Unsaturated Pyrazoleamides with Amidomalonates: Asymmetric Synthesis of (−)-Paroxetine. *Chem. - Eur. J.* **2016**, *22*, 15119. (f) Wang, G. J.; Tang, Y.; Liu, X. H.; Lin, L. L.; Feng, X. M. Enantioselective Synthesis of *N*-H-Free 1,5-Benzothiazepines. *Chem. - Eur. J.* **2017**, *23*, 554.

(16) Stierle, A.; Stierle, D.; Patacini, B. The Berkeleyamides, Amides from the Acid Lake Fungus *Peniciluum rubrum*. *J. Nat. Prod.* **2008**, *71*, 856.

(17) The absolute configuration of berkeleyamide D was determined by comparing the specific rotation with that in ref 8a([α]$^{27}_D$ = + 76.9 (*c* 0.05, MeOH) vs [α]$^{17}_D$ = +84.6 (*c* 0.25, MeOH)). The absolute configuration of **3pf** was determined by the absolute configuration of berkeleyamide D and NOESY correlations.

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