OL Organic Letters

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Letter

Highly Enantioselective Epoxidation of α,β-Unsaturated Ketones Using Amide-Based *Cinchona* Alkaloids as Hybrid Phase-Transfer Catalysts

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Cite This: *Org. Lett.* 2020, 22, 8687−8691

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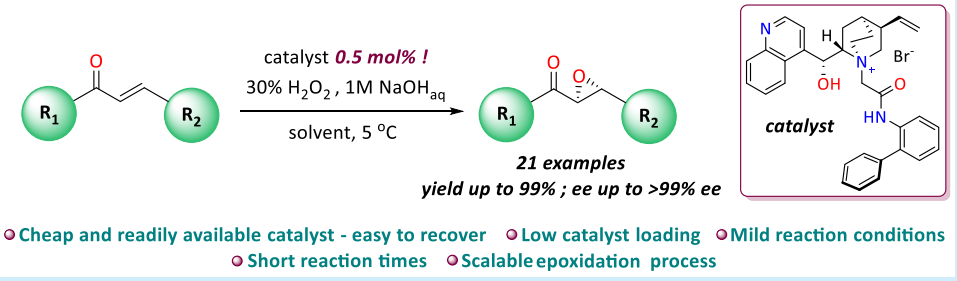


ABSTRACT: A series of 20 one chiral epoxides were obtained with excellent yields (up to 99%) and enantioselectivities (up to >99% ee) using hybrid amide-based *Cinchona* alkaloids. Our method is characterized by low catalyst loading (0.5 mol %) and short reaction times. Moreover, the epoxidation process can be carried out in 10 cycles, without further catalyst addition to the reaction mixture. This methodology significantly enhance the scale of the process using very low catalyst loading.

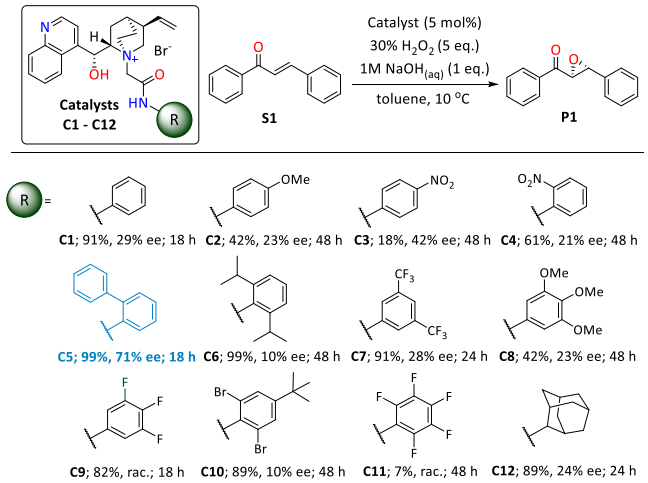
Catalytic enantioselective epoxidation of allylic alcohols, introduced by Sharpless[1] in the 1980s, has been recognized as one of the most significant tools in asymmetric synthesis, since epoxides are considered versatile building blocks and intermediates in asymmetric organic transformations.[2,3] This fundamental discovery has significantly expanded over the last 40 years, especially in the field of metal catalysis[4] and organocatalysis.[5] With the growing demand for green and sustainable chemistry, the development of environmentally benign and cheap catalysts remains a great challenge in stereocontrolled organic synthesis.[6] In this area, phase-transfer catalysis (PTC) has become established as a comprehensive method,[7] owing to mild reaction conditions, operational simplicity, and no use of heavy metals. Particular attention in such work has been devoted to the asymmetric epoxidation of α,β-unsaturated ketones,[3a,8−10] as an extension of the pioneering work by Wynberg et al.[11] on epoxidation of *E*-chalcones using quinine salts as catalysts. However, successful examples of highly enantioselective synthesis of epoxyketones still remain few in number. The most representative continuations of Wynberg's discovery were published in the 1990s by the Lygo[12] and Corey[13] groups. Alternative methods to improving the abilities of *Cinchona*-based catalysts were presented by the Park[14] and Siva[15] groups, who showed that adding surfactants to reaction mixtures or using ultrasound support increased the enantiomeric excess of products formed. On the other hand, Maruoka et al.[16] introduced efficient, but expensive, BINOL-based catalysts. Furthermore, other types of PTC catalysts, such as macrocyclic compounds, peptides, guanidine salts, prolines, etc., have also been used, albeit without high enantioselectivities.[17]

Despite recent spectacular progress in asymmetric epoxidation of *E*-chalcones, there are several issues that prevent their general applicability. The main disadvantages of the methods discussed are as follows: multistep synthesis of catalysts, high catalyst loading, a frequent necessity to use special techniques, and long reaction times. Therefore, there is a strong need for research on rationally designed and efficient PTC catalysts, especially chiral ones, which meet additional requirements related to the possibility of their reuse. Herein, we report our own approach to enantioselective epoxidation by introducing a readily available and finely tunable library of hybrid *Cinchona* alkaloid-based catalysts, the potential application of which we have previously demonstrated in studies on alkylation of imino glycine esters.[18]

We began the present study with epoxidation of model *E*-chalcone **S1** using cinchonidine-based catalyst **C1**, leading to product **P1** with high yield (91%), but low enantioselectivity (29% ee), as shown in Scheme 1. Next, we carried out catalyst screening under the given conditions, and we found that

Received: September 29, 2020
Published: October 28, 2020

Scheme 1. Scope of Hybrid *Cinchona*-Based Catalysts[a]



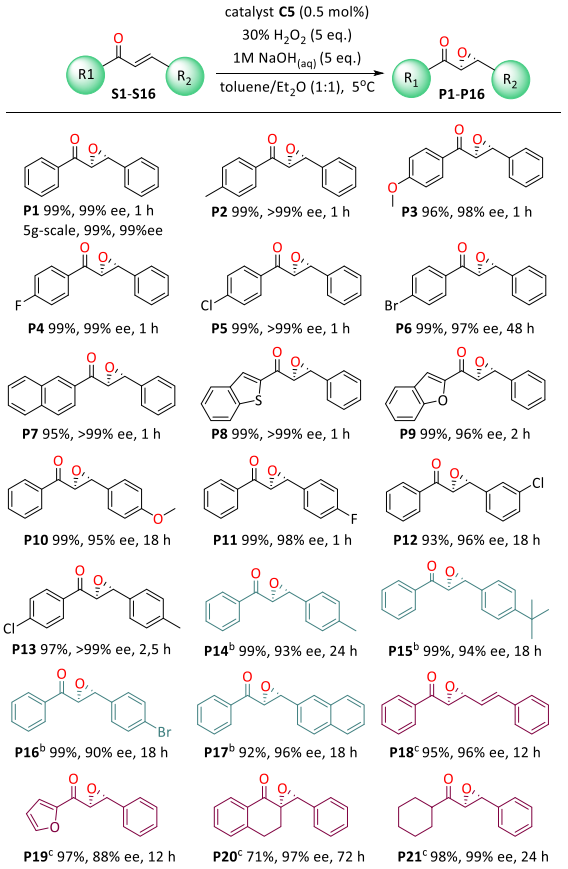
[a]The ee values were determined by HPLC analysis using a chiral column Kromasil OD-H or Chiralcel AD-H and OB-H.

compound **C5** allows the desired epoxides to be obtained with high yield (99%) and promising enantiomeric excess (71% ee). Also, reactions with catalysts based on the other *Cinchona* alkaloids give the desired products with excellent yield, but in racemic form.

Subsequently, we started to optimize the reaction conditions using **C5** as the catalyst, and we noted that the ratio of hydrogen peroxide and aqueous solution of NaOH strongly affected the enantioselectivity. We postulate that the oxidant/base ratio affects the rate of hydrogen peroxide decomposition and formation of the reactive HOO^- ion. Moreover, instead of toluene we found that a mixture of Et_2O/toluene (1:1) was the best solvent for most of these reactions. Finally, we showed that epoxidation of chalcone **S1** under the newly found conditions was very efficient and proceeded for 1 h with an excellent enantiomeric excess (99% ee), using only 0.5 mol % of catalyst at 5 °C temperature. Lower catalyst loading resulted in decreased yield and ee value. All details of the optimization process are presented in the Supporting Information (Tables S2−S6). Under such optimal conditions we examined the reactivity and selectivity of *α,β*-unsaturated ketones **S1−S21** as shown in Scheme 2.

All of the epoxides **P1−P21** were obtained from the corresponding substrates **S1−S21** with both excellent yield and excellent enantioselectivity. For substrates **S1−S13**, with various electron-differentiating substituents on the carbonyl group side, no significant changes in the extremely high selectivities (95−99% ee) were observed. Due to lower solubility of epoxides **P6**, **P10**, and **P12** in the diethyl ether, reactions should be carried out longer (up to 48 h). Slightly lower enantiomeric excesses were noted for epoxidation of *E*-chalcones with an electron-differentiating substituents in the phenyl ring on the double bond side **S14−S17**. In those four cases, achievement of complete conversion required the use of 1 mol % of the catalyst and the reactions were carried out in toluene (**P13−P16** marked green, Scheme 2), but we noted very high yields and ee values (92−99%, 90−96% ee). With more challenging substrates **S18−S21** we performed the epoxidation reactions with 3 mol % of the catalyst **C5** and also in these cases we choose toluene as an optimal solvent (**P18−P21** marked purple, Scheme 2). Epoxidation of **S20** was conducted 72 h

Scheme 2. Asymmetric Epoxidation of *α,β*-Unsaturated Ketones S1−S21 Using Catalyst C5[a]



[a]The ee values were determined by HPLC analysis using a chiral column Kromasil OD-H or Chiralcel AD and OB-H. [b]The ee values were determined by HPLC analysis using a chiral column Kromasil OD-H or Chiralcel AD and OB-H. [c]Reactions were carried out in toluene, and 1 mol % of **C5** was used.

leading to product with moderate yield 71% and high enantiomeric excess 97% ee. It is worth mentioning the great results obtained for (2*E*,4*E*)-1,5-diphenylpenta-2,4-dien-1-one **S18** (95% yield, 96% ee) and *α,β*-unsaturated ketone **S21** containing aliphatic substituent (98% yield, 99% ee). In addition, all epoxides, except **P20**, can be isolated from organic layer using simple filtration by silica gel pad. Such results indicate a fairly universal character of the developed method, and to the best of our knowledge it is a first example of successful epoxidation such substrates using organocatalysts.

The obtained results may indicate a competitive *π*-stacking effect originating from the phenyl system on the double bond side, which may adversely affect the formation of the diastereomeric complex with the catalyst **C5**. In order to explain such high selectivity, we obtained monocrystals of **C5** by slowly evaporation of its saturated solution in wet acetone. Next, we performed a successful single-crystal X-ray diffraction analysis of catalyst **C5** (for details see the Supporting Information), which revealed its distinctive three-dimensional structure (Figure 1).

Let us consider one of the catalyst molecules as it occurs in a single crystal. The **C5** molecule has an aromatic ring stacked in the direction determined by the amide function. Importantly, the arrangement of the phenyl group in the amide arm is nearly perpendicular, this conformational information creating an attractive chiral reaction cavity around the amide function. This

https://dx.doi.org/10.1021/acs.orglett.0c03272
Org. Lett. 2020, 22, 8687−8691

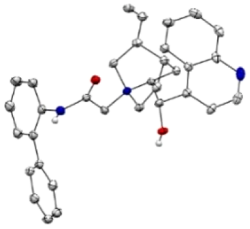


Figure 1. X-ray structure of selected molecule of catalyst **C5**. The solvent molecules, anions, and nonacidic protons were omitted for clarity, and thermal ellipsoids are drawn at the 50% probability level.

strongly implies that the expected hydrogen-bonding interaction would indeed bring an enone inside the cavity to provide an ideal proximity to the hydrogen peroxide ion. This hypothesis is supported by studies with *N*-methylated catalyst **C5** in which we obtained a racemic epoxide **P1**. Our proposed model of the transition state (Figure 2) posits that the chalcone substrate is stabilized by the hydrogen bond from the amide function of a catalyst.

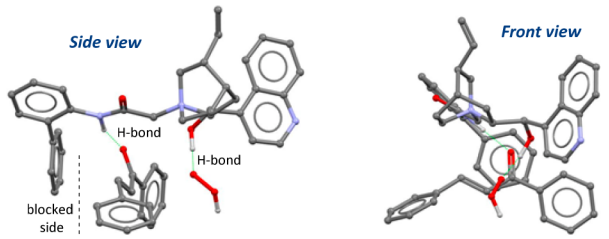


Figure 2. Proposed transition-state model for catalyst **C5** with *E*-chalcone.

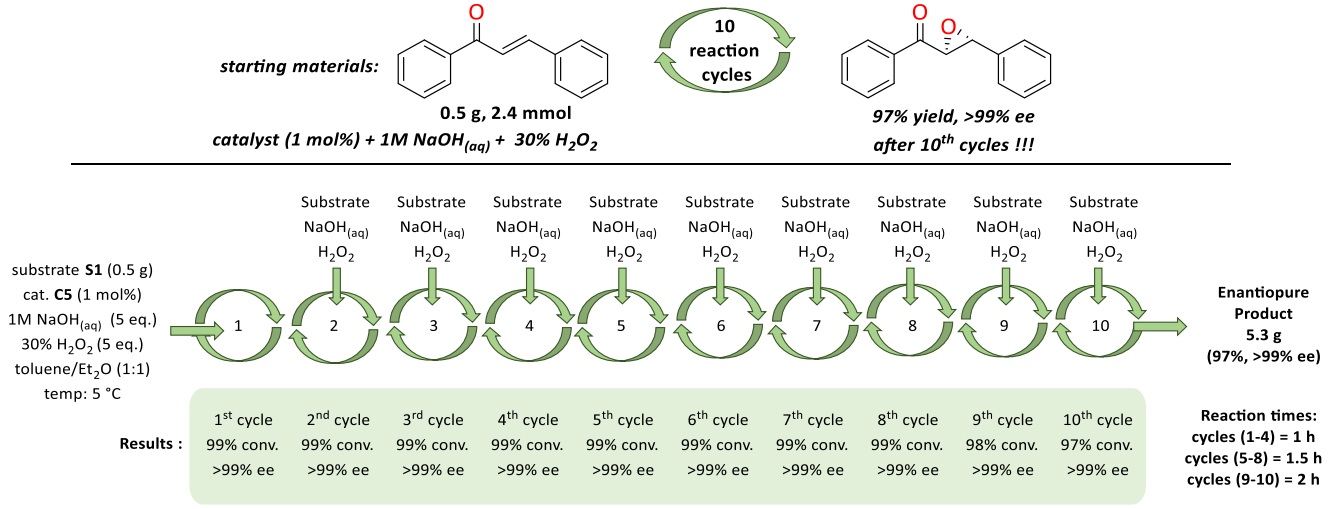
A key element determining the high enantioselection of the reaction is the phenyl ring from the amide arm which has a $\pi-\pi$ stacking interaction with the β-phenyl group of substrate. Such interactions block one of the *E*-chalcone faces. Moreover, the hydroxyl group of the catalyst forms an ionic pair with the hydrogen peroxide ion (HOO^-) via a hydrogen bond. Consequently, the hydrogen peroxide can reach the β-carbon atom of an enone exclusively from above to afford the $\alpha S,\beta R$-product of epoxidation.

The above results turned our attention to the possibility of further improving our reaction. After confirming the stability of catalyst **C5** under PTC-epoxidation conditions, we decided to investigate the possibility of its reuse. Scheme 3 presents our concept of conducting 10 epoxidation cycles under subsequent conditions. The chalcone **S1**, in the presence of 1 mol % of catalyst **C5**, was used for the first reaction cycle.

After completion of the reaction, another portion of hydrogen peroxide and aqueous NaOH, accompanied by chalcone **S1** were added (the second cycle). This procedure was repeated after each reaction cycle in order to maintain full conversion of the reaction. Thus, we were able to carry out epoxidation of chalcone **S1** on a 5 g scale, after 10 reaction cycles, and the product was obtained in total with 97% yield and >99% ee. Note that during eight reaction cycles, the model catalytic reaction did not lose any efficiency or enantioselectivity; however, we terminated the experiment after the tenth cycle due to the slightly lowering of the conversion (to 97%). Given that the epoxidation reaction is very clean, after isolation of the desired product **P1**, we were also able to recover the catalyst **C5** from a postreaction mixture with 99% efficiency, simply by precipitating it with the addition of diethyl ether. Given these advantages, the discussed procedure is an excellent solution for epoxidation on a multigram scale, as only 0.1 mol % of the catalyst was used, based on the final amount of the product obtained. Note that when such catalyst loading under classical batch conditions (without sequential addition of reagents) was used, the products were obtained in the form of a racemate with low yield. Such high efficiency of sequential addition of reagents is observed due to the continuous presence of 1 mol % of catalyst in the reaction mixture, which does not lose its activity over time or in the presence of the product.

In summary, we have developed an efficient method for the preparation of enantiomerically pure epoxyketones using hybrid amide-based *Cinchona* alkaloids as catalysts under PTC conditions. The low loading (0.5 mol %) of highly effective catalysts allowed us to obtain a wide range of such chiral epoxyketones with very high yields and with excellent enantioselectivity (up to 99% and 99% ee, respectively). To the best of our knowledge, these are unique results as compared to those obtained with application of known catalysts, while maintaining such low catalyst loading. Additionally, for the first

Scheme 3. Multigram Synthesis of Epoxide P1 Using Subsequent Epoxidation Reactions



https://dx.doi.org/10.1021/acs.orglett.0c03272
Org. Lett. 2020, 22, 8687−8691

time we presented the possibility of reusing *Cinchona* derivatives in the synthesis of optically pure epoxy ketones by follow-up epoxidation cycles without adding a fresh portion of catalyst between subsequent reactions. This approach could be highly valuable in the synthesis of potential building blocks in the field of medicinal, agrochemical, and material chemistry on a large scale. Further work on applying our catalyst library to asymmetric epoxidation with other enones is in progress.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.orglett.0c03272.

General remarks, experimental procedures, characterization of products, NMR spectra, and HPLC chromatograms (PDF)

Accession Codes

CCDC 2016792 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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Author Contributions

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We acknowledge Poland's National Science Centre (Project 2016/21/B/ST5/03352) for financial support.

■ REFERENCES

(1) (a) Katsuki, T.; Sharpless, K. B. The first practical method for asymmetric epoxidation. *J. Am. Chem. Soc.* **1980**, *102*, 5974−5976. (b) Gao, Y.; Hanson, R. M.; Klunder, J. M.; Ko, S. Y.; Masamune, H.; Sharpless, K. B. Catalytic asymmetric epoxidation and kinetic resolution: modified procedures including in situ derivatization. *J. Am. Chem. Soc.* **1987**, *109*, 5765−5780.

(2) (a) Seayad, J.; List, B. Asymmetric organocatalysis. *Org. Biomol. Chem.* **2005**, *3*, 719−724. (b) Hughes, D. L. Asymmetric Organocatalysis in Drug Development—Highlights of Recent Patent Literature. *Org. Process Res. Dev.* **2018**, *20*, 574−584. (c) Carlone, A.; Bernardi, L. Enantioselective organocatalytic approaches to active pharmaceutical ingredients − selected industrial examples. *Phys. Sci. Rev.* **2019**, *4*, 20180097.

(3) See (a) Gorzynski Smith, J. Synthetically Useful Reactions of Epoxides. *Synthesis* **1984**, 629−656. (b) Lauret, C. Epoxy ketones as versatile building blocks in organic synthesis. *Tetrahedron: Asymmetry* **2001**, *12*, 2359−2383. (c) Marco-Contelles, J.; Molina, M. T.; Anjum, S. Naturally Occurring Cyclohexane Epoxides: Sources, Biological Activities, and Synthesis. *Chem. Rev.* **2004**, *104*, 2857. (d) Miyashita, K.; Imanishi, T. Syntheses of Natural Products Having an Epoxyquinone Structure. *Chem. Rev.* **2005**, *105*, 4515−4536.

(4) (a) Besse, P.; Veschambre, H. Chemical and biological synthesis of chiral epoxides. *Tetrahedron* **1994**, *50*, 8885−8927. (b) Xia, Q.-H.; Ge, H. Q.; Ye, C. P.; Liu, Z. M.; Su, K. X. Advances in Homogeneous and Heterogeneous Catalytic Asymmetric Epoxidation. *Chem. Rev.* **2005**, *105*, 1603−1662. (c) Wang, Ch.; Yamamoto, H. Asymmetric Epoxidation Using Hydrogen Peroxide as Oxidant. *Chem. - Asian J.* **2015**, *10*, 2056−2068.

(5) (a) Adam, W.; Saha-Möller, C. R.; Ganeshpure, P. A. Synthetic Applications of Nonmetal Catalysts for Homogeneous Oxidations. *Chem. Rev.* **2001**, *101*, 3499−3548. (b) Kelly, D. R.; Roberts, S. M. Oligopeptides as catalysts for asymmetric epoxidation. *Biopolymers* **2006**, *84*, 74−89. (c) Wong, O. A.; Shi, Y. Organocatalytic Oxidation. Asymmetric Epoxidation of Olefins Catalyzed by Chiral Ketones and Iminium Salts. *Chem. Rev.* **2008**, *108*, 3958−3987. (d) Lattanzi, A. *Noncovalent Organocatalytic Approach in the Asymmetric Epoxidation of Electron-Poor Alkenes: Recent Developments Frontiers of Green Catalytic Selective Oxidations*; Springer: Singapore, 2019. (e) Triandafillidi, I.; Tzaras, D. I.; Kokotos, Ch. G. Green Organocatalytic Oxidative Methods using Activated Ketones. *ChemCatChem* **2018**, *10*, 2521−2535.

(6) (a) Tavakolian, M.; Vahdati-Khajeh, S.; Asgari, S. Recent Advances in Solvent-Free Asymmetric Catalysis. *ChemCatChem* **2019**, *11*, 2943−2977. (b) Bryliakov, K. P. Catalytic Asymmetric Oxygenations with the Environmentally Benign Oxidants H. *Chem. Rev.* **2017**, *117*, 11406−11459.

(7) For recent reviews on asymmetric phase-transfer catalysis, see: (a) O'Donnell, M. The Enantioselective Synthesis of α-Amino Acids by Phase-Transfer Catalysis with Achiral Schiff Base Esters. *Acc. Chem. Res.* **2004**, *37*, 506. (b) Jew, S-s.; Park, H-h. *Cinchona*-based phase-transfer catalysts for asymmetric synthesis. *Chem. Commun.* **2009**, *14*, 7090−7103. (c) Maruoka, K. Highly practical amino acid and alkaloid synthesis using designer chiral phase transfer catalysts as high-performance organocatalysts. *Chem. Rec.* **2010**, *10*, 254−259. (d) Shirakawa, S.; Maruoka, K. Recent developments in asymmetric phase-transfer reactions. *Angew. Chem., Int. Ed.* **2013**, *52*, 4312−4348. (e) Tan, J.; Yasuda, N. Contemporary Asymmetric Phase Transfer Catalysis: Large-Scale Industrial Applications. *Org. Process Res. Dev.* **2015**, *19*, 1731−1746.

(8) For selected examples, see: (a) Lattanzi, A. Enantioselective Epoxidation of α,β-Enones Promoted by α,α-Diphenyl-l-prolinol as Bifunctional Organocatalyst. *Org. Lett.* **2005**, *7*, 2579−2582. (b) Li, Y.; Liu, X.; Yang, Y.; Zhao, G. 4-Substituted- α,α-diaryl-prolinols Improve the Enantioselective Catalytic Epoxidation of α,β-Enones. *J. Org. Chem.* **2007**, *72*, 288−291. (c) Bondzic, B. P.; Urushima, T.; Ishikawa, H.; Hayashi, Y. Asymmetric Epoxidation of α-Substituted Acroleins Catalyzed by Diphenylprolinol Silyl Ether. *Org. Lett.* **2010**, *12*, 5434−5437.

(9) For selected examples see: (a) Chu, Y. Y.; Liu, X. H.; Li, W.; Hu, X. L.; Lin, L. L.; Feng, X. M. Asymmetric catalytic epoxidation of α,β-unsaturated carbonyl compounds with hydrogen peroxide: Additive-free and wide substrate scope. *Chem. Sci.* **2012**, *3*, 1996−2000. (b) Wang, B.; Miao, C. X.; Wang, S. F.; Xia, C. G.; Sun, W. Manganese Catalysts with C1-Symmetric N4 Ligand for Enantioselective Epoxidation of Olefins. *Chem. - Eur. J.* **2012**, *18*, 6750−6753. (c) Nishikawa, Y.; Yamamoto, H. Iron-Catalyzed Asymmetric Epoxidation of β,β-Disubstituted Enones. *J. Am. Chem. Soc.* **2011**, *133*, 8432−8435. (d) Qian, Q.; Tan, Y.; Zhao, B.; Feng, T.; Shen, Q.; Yao, Y. Asymmetric Epoxidation of Unsaturated Ketones Catalyzed by Heterobimetallic Rare Earth-Lithium Complexes Bearing Phenoxy-Functionalized Chiral Diphenylprolinolate Ligand. *Org. Lett.* **2014**, *16*, 4516−4519. (e) Zeng, C.; Yuan, D.; Zhao, B.; Yao, Y. Highly Enantioselective Epoxidation of α,β-Unsaturated Ketones Catalyzed by Rare-Earth Amides $[(Me_3Si)_2N]_3RE(\mu\text{-Cl})Li(THF)_3$ with Phenoxy-Functionalized Chiral Prolinols *Org. Org. Lett.* **2015**, *17*, 2242−2245.

(10) (a) Reisinger, C. M.; Wang, X.-W.; List, B. Catalytic Asymmetric Hydroperoxidation of α,β-Unsaturated Ketones: An Approach to Enantiopure Peroxyhemiketals, Epoxides, and Aldols. *Angew. Chem.,*

Int. Ed. **2008**, *47*, 8112−8115. (b) Kawai, H.; Okusu, S.; Yuan, Z.; Tokunaga, E.; Yamano, A.; Shiro, M.; Shibata, N. Enantioselective synthesis of epoxides having a tetrasubstituted trifluoromethylated carbon center: methylhydrazine-induced aerobic epoxidation of *β,β*-disubstituted enones. *Angew. Chem., Int. Ed.* **2013**, *52*, 2221−2225.

(11) Hummelen, J. C.; Wynberg, H. Alkaloid assisted asymmetric synthesis IV additional routes to chiral epoxides. *Tetrahedron Lett.* **1978**, *19*, 1089−1092.

(12) (a) Lygo, B.; Wainwright, P. G. Asymmetric phase-transfer mediated epoxidation of *α,β*-unsaturated ketones using catalysts derived from Cinchona alkaloids. *Tetrahedron Lett.* **1998**, *39*, 1599−1602. (b) Lygo, B.; To, D. C. M. Improved procedure for the room-temperature asymmetric phase-transfer mediated epoxidation of *α*, *β*-unsaturated ketones. *Tetrahedron Lett.* **2001**, *42*, 1343−1346. (c) Lygo, B.; Gardiner, S. T.; McLeod, M. C.; To, D. C. M. Diastereo- and enantioselective synthesis of *α,β*-epoxyketones using aqueous NaOCl in conjunction with dihydrocinchonidine derived phase-transfer catalysis at room temperature. Scope and limitations. *Org. Biomol. Chem.* **2007**, *5*, 2283−2290.

(13) Corey, E. J.; Zhang, F.-Y. Mechanism and conditions for highly enantioselective epoxidation of *α*, *β*-enones using charge-accelerated catalysis by a rigid quaternary ammonium salt. *Org. Lett.* **1999**, *1*, 1287−1290.

(14) Jew, S.-s.; Lee, J.-H.; Jeong, B.-S.; Kim, M. J.; Lee, Y.-J.; Lee, J.; Choi, S.-H.; Lee, K.; Lah, M.-S.; Park, H.-g. Highly Enantioselective Epoxidation of 2,4-Diarylenones by Using Dimeric *Cinchona* Phase-Transfer Catalysts: Enhancement of Enantioselectivity by Surfactants. *Angew. Chem., Int. Ed.* **2005**, *44*, 1383−1385.

(15) Sivamani, J.; Ashokkumar, V.; Sadhasivam, V.; Duraimurugan, K.; Siva, A. Ultrasonic assisted dimeric cinchona based chiral phase transfer catalysts for highly enanatioselective synthesis of epoxidation of *α,β*-unsaturated ketones. *RSC Adv.* **2014**, *4*, 60293−60299.

(16) Ooi, T.; Ohara, D.; Tamura, M.; Maruoka, K. Design of New Chiral Phase-Transfer Catalysts with Dual Functions for Highly Enantioselective Epoxidation of *α,β*-Unsaturated Ketones. *J. Am. Chem. Soc.* **2004**, *126*, 6844−6845.

(17) (a) Bakó, T.; Bakó, P.; Keglevich, G.; Bombicz, P.; Kubinyi, M.; Pál, K.; Bodor, S.; Makó, A.; Tőke, L. Phase-transfer catalyzed asymmetric epoxidation of chalcones using chiral crown ethers derived from d-glucose, d-galactose, and d-mannitol. *Tetrahedron: Asymmetry* **2004**, *15*, 1589−1595. (b) Hori, K.; Tamura, M.; Tani, K.; Nishiwaki, N.; Ariga, M.; Tohda, Y. Asymmetric epoxidation catalyzed by novel azacrown ether-type chiral quaternary ammonium salts under phase-transfer catalytic conditions. *Tetrahedron Lett.* **2006**, *47*, 3115−3118. (c) Yoo, M.-S.; Kim, D. G.; Ha, W. M.; Jew, S.-s.; Park, H.-g.; Jeong, B.-S. Synthesis of (*αR,βS*)-epoxyketones by asymmetric epoxidation of chalcones with *Cinchona* phase-transfer catalysts. *Tetrahedron Lett.* **2010**, *51*, 5601.

(18) (a) Majdecki, M.; Niedbała, P.; Jurczak, J. Amide-Based Cinchona Alkaloids as Phase-Transfer Catalysts: Synthesis and Potential Application. *Org. Lett.* **2019**, *21*, 8085−8090. (b) Majdecki, M.; Niedbała, P.; Jurczak, J. Synthesis of C2 Hybrid Amide-Based PTC Catalysts and Their Comparison with Saturated Analogues. *ChemistrySelect* **2020**, *5*, 6424−6429.

https://dx.doi.org/10.1021/acs.orglett.0c03272
Org. Lett. 2020, 22, 8687−8691