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Asymmetric Epoxidation Catalyzed by N-Aryl-Substituted Oxazolidinone-Containing Ketones: Further Evidence for Electronic Effects

Lianhe Shu, Pingzhen Wang, Yonghong Gan, and Yian Shi*

Department of Chemistry, Colorado State University, Fort Collins, Colorado 80523

yian@lamar.colostate.edu

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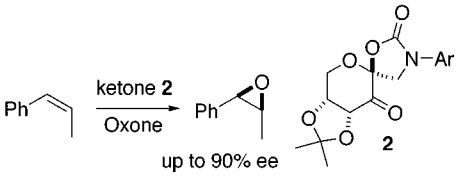
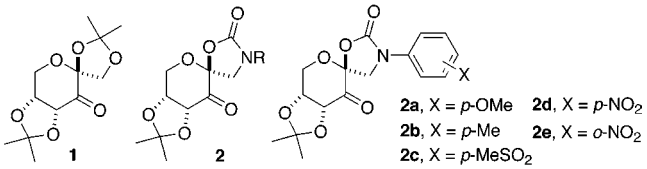
ABSTRACT



Ketones containing N-aryl-substituted oxazolidinones have been prepared and investigated for the epoxidation of *cis*-β-methylstyrene, styrene, and 1-phenylcyclohexene. The attractive interaction between the phenyl group of the olefin and the oxazolidinone of the catalyst is enhanced by introducing an electron-withdrawing group onto the N-phenyl group of the catalyst. The information obtained gives a better understanding of the ketone-catalyzed epoxidation. In addition, the easy preparation of some of the ketones makes them good candidates for practical use.

Asymmetric epoxidation of olefins presents a powerful strategy for the synthesis of enantiomerically enriched epoxides.[1−3] High enantioselectivity has been achieved for the epoxidation of allylic alcohols,[1] the metal-catalyzed epoxidation of unfunctionalized olefins (particularly for conjugated *cis*- and trisubstituted olefins),[2] and the nucleophilic epoxidation of electron-deficient olefins.[3] During the past few years, dioxiranes generated in situ from chiral ketones have shown promise for the asymmetric epoxidation of olefins.[4−6] In our own studies, we have shown that fructose-derived ketone **1** (Scheme 1) is a very effective catalyst for the epoxidaion of *trans*- and trisubstituted olefins.[7] During our recent work, we have found that ketone

Scheme 1



* Phone: 970-491-7424. Fax: 970-491-1801.

(1) For recent reviews on highly enantioselective epoxidation of allylic alcohols, see: (a) Johnson, R. A.; Sharpless, K. B. In *Catalytic Asymmetric Synthesis*; Ojima, I., Ed.; VCH: New York, 1993; Chapter 4.1. (b) Katsuki, T.; Martin, V. S. *Org. React*. **1996**, *48*, 1. (c) Johnson, R. A.; Sharpless, K. B. In *Catalytic Asymmetric Synthesis*; Ojima, I., Ed.; VCH: New York, 2000; Chapter 6A.

(2) For recent reviews on metal-catalyzed highly enantioselective epoxidation of unfunctionalized olefins, see: (a) Jacobsen, E. N. In *Catalytic Asymmetric Synthesis*; Ojima, I., Ed.; VCH: New York, 1993; Chapter 4.2. (b) Collman, J. P.; Zhang, X.; Lee, V. J.; Uffelman, E. S.; Brauman, J. I. *Science* **1993**, *261*, 1404. (c) Mukaiyama T. *Aldrichimica Acta* **1996**, *29*, 59. (d) Katsuki, T. In *Catalytic Asymmetric Synthesis*; Ojima, I., Ed.; VCH: New York, 2000; Chapter 6B.

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(4) For general leading references on dioxiranes, see: (a) Murray, R. W. *Chem. Rev*. **1989**, *89*, 1187. (b) Adam, W.; Curci, R.; Edwards, J. O. *Acc. Chem. Res*. **1989**, *22*, 205. (c) Curci, R.; Dinoi, A.; Rubino, M. F. *Pure Appl. Chem*. **1995**, *67*, 811. (d) Clennan, E. L. *Trends Org. Chem.* **1995**, *5*, 231. (e) Adam, W.; Smerz, A. K. *Bull. Soc. Chim. Belg*. **1996**, *105*, 581.

(5) For recent reviews on chiral ketone-catalyzed asymmetric epoxidation, see: (a) Denmark, S. E.; Wu, Z. *Synlett* **1999**, 847. (b) Frohn, M.; Shi, Y. *Synthesis* **2000**, 1979.

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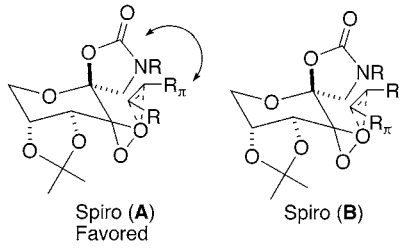
2 containing an oxazolidinone provides encouragingly high ees for the epoxidation of *cis*-olefins and styrenes.[8] Our earlier studies suggest that electronic interactions play an important role in stereodifferentiation. It appears that there is an attractive interaction between the R_π group and the oxazolidinone moiety of the ketone catalyst in the transition state (Scheme 2).[9,10] As a result, groups with π systems (R_π)

Scheme 2

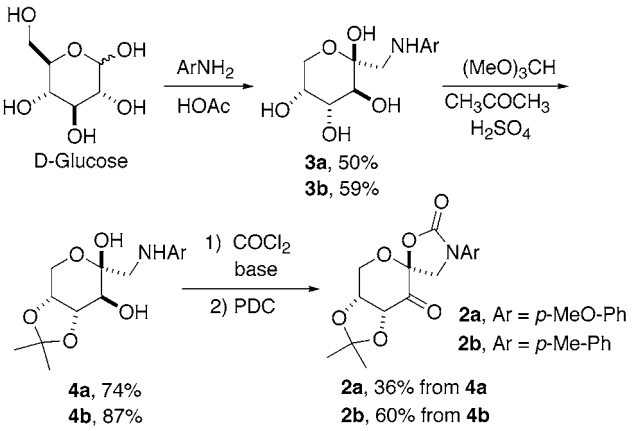


could be significantly differentiated from those without π electrons (R), leading to high enantioselectivity for the reaction.

Our studies have also shown that the substituents on the nitrogen of the ketone catalyst have a significant effect on the enantioselectivity of the epoxidation.[8c] The influence of the N-substituents on the enantioselectivity is believed to be electronic rather than steric in nature.[8c] To further probe the interaction, ketones **2a**−**e** (Scheme 1) with substituents on the phenyl group were prepared, and the effect of varying the substituents on the enantioselectivity of the epoxidation was studied. Herein, we report our preliminary efforts on this subject.

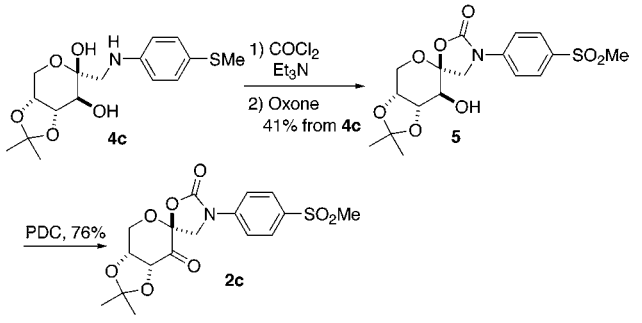
The syntheses of ketones **2a**−**e** are outlined in Schemes 3−5. Briefly, ketones **2a**,**b** were prepared from D-glucose

Scheme 3



by the Amadori rearrangement,[11] ketalization, oxazolidinone formation, and PDC oxidation in 13 and 31% overall yields, respectively (Scheme 3). Ketone **2c** was prepared in a manner similar to **2a**,**b**, except that the sulfide was oxidized to the sulfone before the PDC oxidation of the alcohol (Scheme 4). Ketones **2d**−**e** were prepared from compound **6**[8c] by a

Scheme 4



nucleophilic aromatic substitution, desilylation, and PDC oxidation (Scheme 5). Among these ketones, crystal structures of **2a**−**b** were obtained and showed that the phenyl groups in these ketones are coplanar with the oxazolidinones.

The catalytic properties of ketones **2a**−**e** were then investigated using *cis*-β-methylstyrene, styrene, and 1-phen-

(6) For leading references on asymmetric epoxidation mediated in situ by chiral ketones, see: (a) Curci, R.; Fiorentino, M.; Serio, M. R. *J. Chem. Soc., Chem. Commun*. **1984**, 155. (b) Curci, R.; D'Accolti, L.; Fiorentino, M.; Rosa, A. *Tetrahedron Lett*. **1995**, *36*, 5831. (c) Denmark, S. E.; Forbes, D. C.; Hays, D. S.; DePue, J. S.; Wilde, R. G. *J. Org. Chem*. **1995**, *60*, 1391. (d) Brown, D. S.; Marples, B. A.; Smith, P.; Walton, L *Tetrahedron* **1995**, *51*, 3587. (e) Yang, D.; Yip, Y. C.; Tang, M. W.; Wong, M. K.; Zheng, J. H.; Cheung, K. K. *J. Am. Chem. Soc*. **1996**, *118*, 491. (f) Yang, D.; Wang, X.-C.; Wong, M.-K.; Yip, Y.-C.; Tang, M.-W. *J. Am. Chem. Soc*. **1996**, *118*, 11311. (g) Song, C. E.; Kim, Y. H.; Lee, K. C.; Lee, S. G.; Jin, B. W. *Tetrahedron: Asymm*etry **1997**, *8*, 2921. (h) Adam, W.; Zhao, C.-G. *Tetrahedron: Asymmetry* **1997**, *8*, 3995. (i) Denmark, S. E.; Wu, Z.; Crudden, C. M.; Matsuhashi, H. *J. Org. Chem*. **1997**, *62*, 8288. (j) Wang, Z.-X.; Shi, Y. *J. Org. Chem*. **1997**, *62*, 8622. (k) Adam, W.; Fell, R. T.; Saha-Moller, C. R.; Zhao, C.-G. *Tetrahedron: Asymmetry* **1998**, *9*, 397. (l) Armstrong, A.; Hayter, B. R. *Chem. Commun*. **1998**, 621. (m) Yang, D.; Wong, M.-K.; Yip, Y.-C.; Wang, X.-C.; Tang, M.-W.; Zheng, J.-H.; Cheung, K.-K. *J. Am. Chem. Soc*. **1998**, *120*, 5943. (n) Yang, D.; Yip, Y.-C.; Chen, J.; Cheung, K.-K. *J. Am. Chem. Soc*. **1998**, *120*, 7659. (o) Adam, W.; Saha-Moller, C. R.; Zhao, C.-G. *Tetrahedron: Asymmetry* **1999**, *10*, 2749. (p) Carnell, A. J.; Johnstone, R. A. W.; Parsy, C. C.; Sanderson, W. R. *Tetrahedron Lett*. **1999**, *40*, 8029. (q) Armstrong, A.; Hayter, B. R. *Tetrahedron* **1999**, *55*, 11119. (r) Armstrong, A.; Hayter, B. R.; Moss, W. O.; Reeves, J. R.; Wailes, J. S. *Tetrahedron: Asymmetry* **2000**, *11*, 2057. (s) Solladie-Cavallo, A.; Bouerat, L. *Org. Lett*. **2000**, *2*, 3531. (t) Bortolini, O.; Fogagnolo, M.; Fantin, G.; Maietti, S.; Medici, A. *Tetrahedron: Asymmetry* **2001**, *12*, 1113. (u) Seki, M.; Furutani, T.; Imashiro, R.; Kuroda, T.; Yamanaka, T.; Harada, N.; Arakawa, H.; Kusama, M.; Hashiyama, T. *Tetrahedron Lett*. **2001**, *42*, 8201. (v) Armstrong, A.; Moss, W. O.; Reeves, J. R. *Tetrahedron: Asymmetry* **2001**, *12*, 2779. (w) Matsumoto, K.; Tomioka, K. *Tetrahedron Lett*. **2002**, *43*, 631. (x) Stearman, C. J.; Behar, V. *Tetrahedron Lett*. **2002**, *43*, 1943. (y) Denmark, S. E.; Matsuhashi, H. *J. Org. Chem*. **2002**, *67*, 3479. (z) Shing, T. K. M.; Leung, G. Y. C. *Tetrahedron* **2002**, *58*, 7545.

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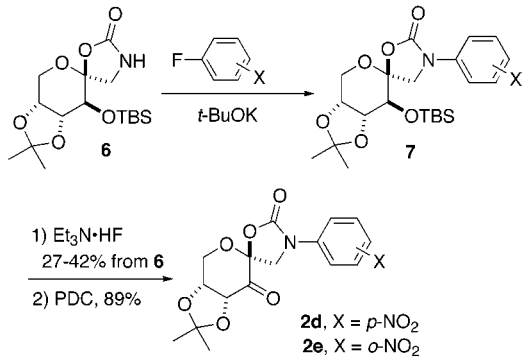
(8) (a) Tian, H.; She, X.; Shu, L.; Yu, H.; Shi, Y. *J. Am. Chem. Soc*. **2000**, *122*, 11551. (b) Tian, H.; She, X.; Xu, J.; Shi, Y. *Org. Lett*. **2001**, *3*, 1929. (c) Tian, H.; She, X.; Yu, H.; Shu, L.; Shi, Y. *J. Org. Chem*. **2002**, *67*, 2435.

(9) Other nonbonding interactions such as hydrophobic interactions could also contribute to the observed enantioselectivity.

(10) For an observation of electronic interaction in ketone-catalyzed asymmetric epoxidation, see ref 6n.

(11) Hodge, J. E.; Fisher, B. E. *Methods Carbohydr. Chem*. **1963**, *2*, 99.

Scheme 5



ylcyclohexene as substrates. As shown in Table 1, in the case of *cis*-β-methylstyrene, the ee increased from 83 to 90% from the electron-donating MeO group to the electron-withdrawing sulfone and nitro groups. These results suggest

Table 1. Asymmetric Epoxidation of Olefins Catalyzed by Ketones **2a**−**e**[a]

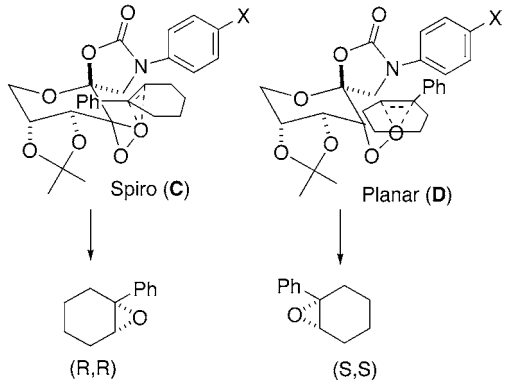
Entry	Ketone	Ph	Ph	Ph
		Conv. (ee) (%)[b]	Conv. (ee) (%)[b]	Conv. (ee) (%)[b]
1	**2a**	71 (83) (2R,3S)	56 (80) (R)	53 (26) (R,R)
2	**2b**	60 (84) (2R,3S)	60 (80) (R)	61 (25) (R,R)
3	**2c**	72 (90) (2R,3S)	61 (80) (R)	58 (22) (S,S)
4	**2d**	55 (90) (2R,3S)	30 (79) (R)	64 (27) (S,S)
5	**2e**	59 (78) (2R,3S)	55 (62) (R)	48 (59) (R,R)

[a] All reactions were carried out with olefin (0.2 mmol), ketone (0.02 mmol), Oxone (0.356 mmol), and K_2CO_3 (0.804 mmol) in DME/DMM (3:1, v/v) (3 mL) and buffer (0.2 M K_2CO_3−AcOH, pH 8.0) (2 mL) at −10 °C. Reactions were stopped after 3.5 h. [b] Conversion and enantioselectivity were determined by chiral GC (Chiraldex B-DM).

that the interactions between the phenyl group of the olefin and the oxazolidinone moiety of the catalyst in transition state spiro **A** (Scheme 2) are influenced by the electronic nature of the substituents on the N-phenyl groups and favored by electron-withdrawing groups. The lower ee obtained with **2e** is probably due to the fact the N-phenyl group in **2e** is no longer coplanar with the oxazolidinone due to the presence of the *ortho* nitro group on the phenyl group.

The substituent effect on the enantioselectivity is even more explicitly displayed in the epoxidation of 1-phenylcyclohexene. As shown in Table 1, the (*R*,*R*)-isomer was obtained with *p*-MeO and *p*-Me groups, and the (*S*,*S*)-isomer was obtained with *p*-$MeSO_2$ and *p*-NO_2 groups, indicating that planar **D** became a major transition state when electron-withdrawing groups were attached to the N-phenyl group of the catalyst (Scheme 6).[8c] Clearly, electron-withdrawing groups on the N-phenyl group of the catalyst further enhance the attractive interactions between the phenyl groups of the

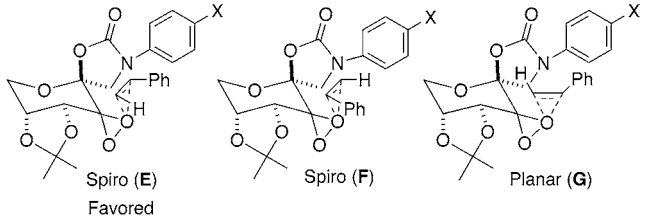
Scheme 6



olefins and the oxazolidinones of the catalyst in the transition state. These results, along with our earlier observations,[8c] suggest that the attractive interaction between the R_π group and the oxazolidinone moiety of the ketone catalyst in the transition state (Scheme 2) can be strengthened by a group that can withdraw electrons from the oxazolidinone through conjugation.

It is interesting that in the case of styrene, the ee remained the same (79−80%) regardless of whether an electron-donating or electron-withdrawing group was attached to the N-phenyl group of the catalyst. Our earlier studies suggest that in addition to spiro **F**, transition state planar **G** is also competing with the favored transition state spiro **E** (Scheme 7).[8b,c] The introduction of an electron-withdrawing group onto

Scheme 7



the N-phenyl of the catalyst enhances the interaction between the phenyl group of the olefin and the oxazolidinone of the catalyst in both spiro **E** and planar **G**. As a result, no net increase in enantioselectivity is observed. This result suggests that the major competing transition state for styrene is planar **G** rather than spiro **F**.

In summary, the asymmetric epoxidation of olefins using N-aryl-substituted oxazolidinone-containing ketones **2a**−**e** as catalysts has been investigated. The results show that the attractive interaction between the phenyl group of the olefin and the oxazolidinone of the catalyst is enhanced by introducing an electron-withdrawing group onto the N-phenyl group of the catalyst. The information obtained in this study gives a better understanding of the factors involved in ketone-catalyzed epoxidation and provides useful insight for design-

ing new catalysts. In addition, the easy preparation of some of the ketones makes them good candidates for practical use.

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Supporting Information Available: Epoxidation procedure, syntheses of ketone catalysts, and GC data for the determination of the enantiomeric excess of the epoxides. This material is available free of charge via the Internet at http://pubs.acs.org.

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