Kinetic Resolution of Acyclic Secondary Allylic Silyl Ethers Catalyzed by Chiral Ketones

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Kinetic resolution of acyclic secondary allylic silyl ethers by chiral dioxiranes generated in situ from chiral ketones (*R*)-**1** and (*R*)-**2** and Oxone was investigated. An efficient and catalytic method has been developed for kinetic resolution of those substrates with a CCl_3, *tert*-butyl, or CF_3 group at the α-position. In particular, high selectivities (*S* up to 100) were observed for kinetic resolutions of racemic α-trichloromethyl allylic silyl ethers **7** and **9**−**15** catalyzed by ketones (*R*)-**2**. Both the recovered substrates and the resulting epoxides were obtained in high enantiomeric excess. On the basis of steric and electrostatic interactions between the chiral dioxiranes and the racemic substrates, a model was proposed to rationalize the enantioselectivities and diastereoselectivities in the chiral ketone-catalyzed kinetic resolution process.

Introduction

Both chiral secondary allylic alcohols[1] and the corresponding chiral epoxy alcohols[1b] are versatile building blocks for asymmetric synthesis of biologically active natural products. Kinetic resolution[2−4] of readily available racemic secondary allylic alcohols or their derivatives via an enantioselective epoxidation method, e.g., Sharpless asymmetric epoxidation method,[4a,b] offers a feasible and efficient access to both kinds of chiral intermediates. In recent years, chiral ketones have been found to be efficient catalysts for asymmetric epoxidation of *trans*-olefins and trisubstituted olefins.[5] Thus, chiral dioxiranes are expected to be sensitive to the preexisting chirality in secondary allylic alcohols or their derivatives, which is essential to the kinetic resolution. Herein we report our results on chiral ketone-catalyzed kinetic resolution of acyclic secondary allylic silyl ethers.

Results and Discussions

I. Resolutions of Racemic α-Trichloromethyl Allylic Alcohols and Their Derivatives. Our initial attention was drawn to the resolution of α-trichloromethyl allylic alcohols and their derivatives for two reasons. First, this particular class of chiral allylic alcohols not only are important intermediates in the synthesis of natural products of agricultural importance, e.g., sodium cilastatin,[6a] NRDC 182,[6b,c] permethrin,[6b] decamethrin,[6b] and cypermethrin,[6c] but also can be easily transformed to other useful products such as allylic thiols,[7a,b] terminal vinyl epoxides,[7c] α-fluoro acids,[7d] hydroxy acids,[7e,f] and amino acids.[7e,f] Second, a number of methods have been developed to conveniently prepare racemic α-trichloromethyl allylic alcohols, e.g., via nucleophilic addition to α,β-unsaturated aldehydes by trichloromethide, which can be generated from a 1:1 mixture of trichloroacetic acid and sodium trichloroacetate in dimethylformamide,[8a] cathodic reduction of carbon tetrachloride,[8b] or decomposition of trichloroacetic acid in hexamethylphosphoric triamide.[8c] However, preparation of enantiomerically

(1) (a) Wipf, P. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: Oxford, 1991; Vol. 5, p 827. (b) Johnson, R. A.; Sharpless, K. B. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: Oxford, 1991; Vol. 7, p 389. (c) Lipshutz, B. H.; Sengupta, S. In *Organic Reactions*; Wiley: New York, 1992; Vol. 41, p 135.

(2) For recent reviews of kinetic resolution, see: (a) Kagan, H. B.; Fiaud, J. C. *Top. Stereochem.* **1988**, *18*, 249. (b) Finn, M. G.; Sharpless, K. B. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press: New York, 1985; p 247.

(3) For selected examples on kinetic resolution of cyclic allylic alcohols and/or their derivatives, see: (a) Visser, M. S.; Harrity, J. P. A.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1996**, *118*, 3779. (b) Kitamura, M.; Kasahara, I.; Manabe, K.; Noyori, R. *J. Org. Chem.* **1988**, *53*, 708. (c) Kolb, H. C.; VanNieuwenhze, M. S.; Sharpless, K. B. *Chem. Rev.* **1994**, *94*, 2483. (d) Frohn, M.; Zhou, X.; Zhang, J.-R.; Tang, Y.; Shi, Y. *J. Am. Chem. Soc.* **1999**, *121*, 7718.

(4) For selected examples on kinetic resolution of acyclic allylic alcohols and/or their derivatives, see: (a) Martin, V. S.; Woodard, S. S.; Katsuki, T.; Yamada, Y.; Ikeda, M.; Sharpless, K. B. *J. Am. Chem. Soc.* **1981**, *103*, 6237. (b) Gao, Y.; Hanson, R. M.; Klunder, J. M.; Ko, S. Y.; Masamune, H.; Sharpless, K. B. *J. Am. Chem. Soc.* **1987**, *109*, 5765. (c) Vedejs, E.; Chen, X. *J. Am. Chem. Soc.* **1996**, *118*, 1809. (d) Ruble, J. C.; Latham, H. A.; Fu, G. C. *J. Am. Chem. Soc.* **1997**, *119*, 1492. (e) Burgess, K.; Jennings, L. D. *J. Am. Chem. Soc.* **1991**, *113*, 6129.

(5) For selected examples of asymmetric epoxidation mediated by chiral ketones, see: (a) Curci, R.; D′Accolti, L.; Fiorentino, M.; Rosa, A. *Tetrahedron Lett.* **1995**, *36*, 5831. (b) Yang, D.; Yip, Y.-C.; Tang, M.-W.; Wong, M.-K.; Zheng, J.-H.; Cheung, K.-K. *J. Am. Chem. Soc.* **1996**, *118*, 491. (c) Yang, D.; Wang, X.-C.; Wong, M.-K.; Yip, Y.-C.; Tang, M.-W. *J. Am. Chem. Soc.* **1996**, *118*, 11311. (d) 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. (e) Tu, Y.; Wang, Z.-X.; Shi, Y. *J. Am. Chem. Soc.* **1996**, *118*, 9806. (f) Wang, Z.-X.; Tu, Y.; Frohn, M.; Zhang, J.-R.; Shi, Y. *J. Am. Chem. Soc.* **1997**, *119*, 11224. (g) Tian, H.; She, X.; Shu, L.; Yu, H.; Shi, Y. *J. Am. Chem. Soc.* **2000**, *122*, 11551. (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) Armstrong, A.; Hayter, B. R. *J. Chem. Soc., Chem. Commun.* **1998**, 621.

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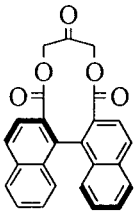
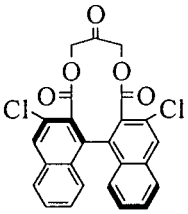
Chart 1

Ketones:

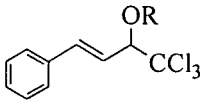


(*R*)-**1**

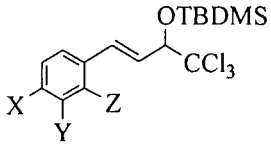


(*R*)-**2**

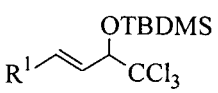
Substrates:



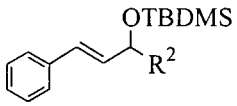
3 R = H
4 R = Ac
5 R = COPh
6 R = TMS
7 R = TBDMS
8 R = TBDPS



9 X = Me, Y = H, Z = H
10 X = Et, Y = H, Z = H
11 X = *i*Pr, Y = H, Z = H
12 X = *t*Bu, Y = H, Z = H
13 X = MeO, Y = H, Z = H
14 X = Cl, Y = H, Z = H
15 X = CF_3, Y = H, Z = H
16 X = H, Y = Me, Z = H
17 X = H, Y = CF_3, Z = H
18 X = H, Y = H, Z = Me



19 R^1 = 
20 R^1 = nC_5H_{11}



21 R^2 = *t*Bu
22 R^2 = CF_3
23 R^2 = Ph

pure or enriched α-trichloromethyl allylic alcohols remains a challenge for organic chemists and there is no general and catalytic method available except one enzymatic approach.[6c]

(1) Effect of Protecting Groups on the Resolution Efficiencies. We reported that C_2 symmetric chiral ketones (*R*)-**1** and (*R*)-**2** (Chart 1) were efficient catalysts for asymmetric epoxidation of unfunctionalized olefins, especially *trans*-stilbenes.[5b−d] Recent efforts made it possible to prepare these ketones on a large scale.[9] We first examined the kinetic resolution of racemic α-trichloromethyl allylic alcohol **3** mediated by the chiral dioxirane generated in situ from Oxone and readily available ketone (*R*)-**1**, and found, unfortunately, the resolution efficiency to be rather poor (S = 1.3, entry 1, Table 1). We reasoned that the low selectivity could be due to the small size of the OH group on substrate **3**. The OH group was then protected as acetate, benzoyl ester, or TMS, TBDMS, and TBDPS ethers, and the resulting substrates **4**−**8** were subjected to the kinetic resolution conditions. We found that substrates of smaller OR group, such as OH, acetate, benzoyl ester, and OTMS, gave lower S values (entries 2−4), while very bulky groups such as OTBDPS almost prohibited the reaction (conversion <5% after 24 h, entry 6). The OTBDMS group was found to be the best one in terms of resolution efficiency (entry 5).

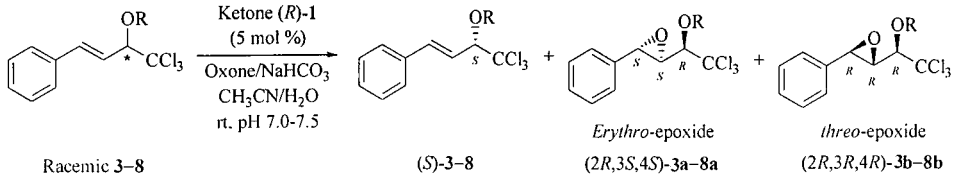
(2) Resolutions of α-Trichloromethyl Allylic TBDMS Ethers Catalyzed by Ketones (*R*)-1 and (*R*)-2. Encouraged by the above results, a variety of TBDMS-protected α-trichloromethyl allylic alcohols **7** and **9**−**20** were prepared and subjected to the kinetic resolution conditions with ketones (*R*)-**1** and (*R*)-**2** as catalysts (5 mol % loading). The results are summarized in Table 2. The recovered starting materials were enriched in the (*S*)-enantiomers, the configuration of which was determined by Mosher's method.[10] The resulting epoxides had the (*R*)-configuration at the C-2 position as determined by X-ray crystallography.[11] It was found that both steric and electronic effects played important roles in determining the resolution efficiency. Generally, higher selectivities were obtained for substrates of bulkier *para* substituents on the phenyl ring of the substrates (Table 2, entries 2−5 vs 1 and 13−16 vs 12). A *m*-methyl group on the phenyl ring did not significantly change the resolution efficiency (entry 9 vs 1). The steric effect was

(9) For convenient preparations of enantiopure ketones (*R*)-**1** and (*R*)-**2** on a large scale, see: (a) Seki, M.; Furutani, T.; Hatsuda, M.; Imashiro, R. *Tetrahedron Lett.* **2000**, *41*, 2149. (b) Kuroda, T.; Imashiro, R.; Seki, M. *J. Org. Chem.* **2000**, *65*, 4213.

(10) (a) Dale, J. A.; Dull, D. L.; Mosher, H. S. *J. Org. Chem.* **1969**, *34*, 2543. (b) Dale, J. A.; Mosher, H. S. *J. Am. Chem. Soc.* **1973**, *95*, 512.

(11) The *erythro*-epoxides **12a**, **14a**, and **15a** were found to have the (*S*,*S*,*R*) configuration by X-ray analysis. Other *erythro*-epoxides **7a**, **9a**−**11a**, **13a**, and **16a**−**20a** were assumed to have the same absolute configuration as that of **12a**, **14a**, and **15a**.

Table 1. Effect of Protecting Group on Efficiencies of Kinetic Resolution Catalyzed by Ketone (*R*)-1[a,b]



				recovd SM		epoxide		
entry	substrate	time (h)	convn (%)[c]	yield (%)[d]	ee (%)[e,f]	*E*/*T* ratio[g]	yield (%)[d]	*S*[h]
1	**3**	4	75	80	16 (*S*)	3:1	85	1.3
2	**4**	3	81	88	13	1.2:1	82	1.2
3	**5**	4	70	86	3	1.1:1	83	1.1
4	**6**	24	50	86	27 (*S*)	>49:1	80	2
5	**7**	24	56	81	70 (*S*)	>49:1	78	7
6	**8**	24	<5	*i*	*i*	*i*	*i*	*i*

[a] Reaction conditions were as follows: room temperature, 0.2 mmol of substrate, 0.01 mmol of ketone (*R*)-**1**, 0.5 mmol of Oxone, 1.55 mmol of $NaHCO_3$, 1.5 mL of CH_3CN, and 1 mL of aqueous Na_2·EDTA solution (4×10^{-4} M) [b] (*R*)-**1**: 98% ee. Ketone (*R*)-**1** was recovered in over 80% yield by flash column chromatography and reused without loss of catalytic activity and chiral induction. [c] Conversion was determined by ^{1}H NMR of the crude reaction mixture after workup. [d] Yield based on the conversion. [e] The ee value was determined by HPLC (Chiralcel OD column). [f] The absolute configuration was determined by Mosher's method. [g] The ratio of *erythro*/*threo*-epoxides was determined by ^{1}H NMR. [h] The selectivity (*S*) was calculated by the equation $S = \ln[(1 - C)(1 - \text{ee})]/\ln[(1 - C)(1 + \text{ee})]$, where *C* is conversion and ee is percentage enantiomeric excess of the recovered substrate. [i] Not determined.

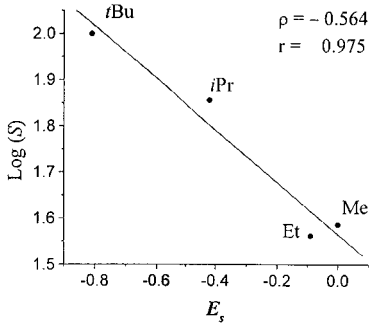


Figure 1. Hammett plot of the logarithm of selectivity (*S*), obtained with ketone (*R*)-**2** as the catalyst, against the Taft steric substituent constants E_s.

further confirmed by a linear Hammett plot ($\rho = -0.564$, $r = 0.975$) of the logarithm of the *S* values, obtained with ketone (*R*)-**2** as the catalyst, against the Taft steric substituent constants E_s[12] of *para* substituents on substrates **9**−**12** (Me, Et, *i*Pr, and *t*Bu groups) (Figure 1). On the other hand, substrates with electron-donating groups on the phenyl ring always gave higher selectivities than those with electron-withdrawing groups (entries 7 vs 6, 9 vs 10, and 17 vs 18). As expected, ketone (*R*)-**2** gave a much higher selectivity than ketone (*R*)-**1** for resolution of the same substrate (entries 1−8 and 12−19).

Two additional features of the present kinetic resolution method are worth noting. First, the present method was more effective for resolution of substrates with an aryl group on the double bond than those with an alkyl group (entries 12−19 vs 20 and 21). In particular, the *S* values ranged from 18 to 100 for resolution of substrates **7** and **9**−**15** with ketone (*R*)-**2** as the catalyst. Second, the present kinetic resolution method showed very high diastereoselectivities. Almost a single diastereomeric epoxide was exclusively formed with ratios of *erythro*/*threo*-epoxides over 49:1.[11] The *erythro*-epoxides also showed reasonably high enantiomeric excesses (77−93% ee; Table 2, entries 12−16).

(12) Taft, R. W., Jr. *J. Am. Chem. Soc.* **1952**, *74*, 3120.

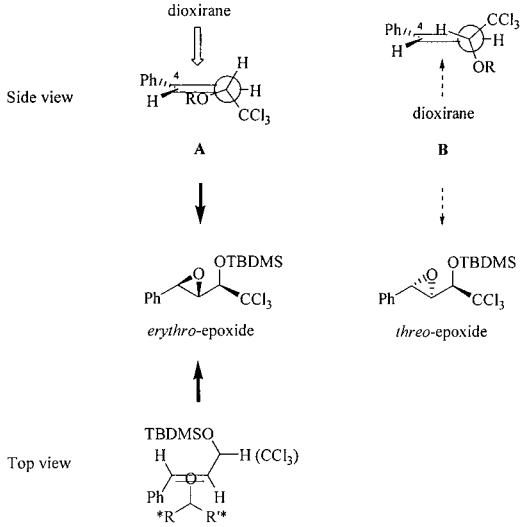


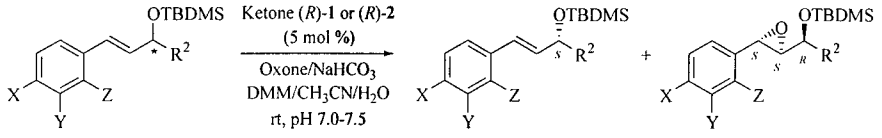
Figure 2. The most stable conformers **A** and **B** of substrate **7**.

(3) Transition States for Kinetic Resolution of Substrates 7 and 9−20 Catalyzed by Ketones (*R*)-1 and (*R*)-2. The most stable conformers of substrate **7**, namely **A** (∠OCC=C about 0°) and **B** (∠OCC=C about 120°), were located by using the MacroModel program[13] (Figure 2). The free energies of **A** and **B** were comparable ($\Delta G°_{rel} = 0.1$ kcal/mol) but much lower than those of other conformers (structure not shown) by >20 kcal/mol. As shown in Figure 2, in the kinetic resolution process, the bulky CCl_3 group in conformers **A** and **B** could shield one face of the olefinic double bond and is thus *anti* to the approaching dioxirane in the transition states.[14] The

(13) MacroModel version 4.5: Mohamadi, F.; Richards, N. G. J.; Guida, W. C.; Liskamp, R.; Lipton, M.; Caufield, C.; Chang, G.; Hendrickson, T.; Still, W. C. *J. Comput. Chem.* **1990**, *11*, 440.

(14) Theoretical studies by Houk et al. indicated that stereoselective attack of an electrophilic reagent to acyclic chiral olefins, with different substituents on the allylic position, preferentially passes through the "staggered" or "*anti*-periplanar" transition states which have the largest group *anti* to the partially formed bonds. See: (a) Houk, K. N.; Moses, S. R.; Wu, Y.-D.; Rondan, N. G.; Jäger, V.; Schohe, R.; Fronczek, F. R. *J. Am. Chem. Soc.* **1984**, *106*, 3880. (b) Houk, K. N.; Duh, H.-Y.; Wu, Y.-D.; Moses. S. R. *J. Am. Chem. Soc.* **1986**, *108*, 2754.

Table 2. Kinetic Resolution of Acyclic Secondary Allylic Silyl Ethers Catalyzed by Ketones (*R*)-1 and (*R*)-2[a]



					recovd SM		epoxide			
entry	substrate	ketone[b]	time (h)	convn (%)[c]	yield (%)[d]	ee (%)[e,f]	*E*/*T* ratio[g]	yield (%)[d]	ee (%)[h]	S[i]
1	**7**	(*R*)-**1**	24	56	81	70 (*S*)	>49:1	78	*j*	7
2	**9**	(*R*)-**1**	24	53	90	65 (*S*)	>49:1	83	*j*	7
3	**10**	(*R*)-**1**	24	56	65	64 (*S*)	>49:1	69	*j*	6
4	**11**	(*R*)-**1**	24	53	82	79 (*S*)	>49:1	88	*j*	13
5	**12**	(*R*)-**1**	24	63	84	96 (*S*)	>49:1	82	*j*	13
6	**13**	(*R*)-**1**	24	66	83	98 (*S*)	>49:1	52	*j*	13
7	**14**	(*R*)-**1**	44	59	55	75 (*S*)	>49:1	51	*j*	7
8	**15**	(*R*)-**1**	24	32	84	38 (*S*)	>49:1	76	*j*	13
9	**16**	(*R*)-**1**	24	55	60	66 (*S*)	>49:1	64	*j*	6
10	**17**	(*R*)-**1**	48	49	75	30 (*S*)	>49:1	88	*j*	2
11	**18**	(*R*)-**1**	24	53	67	46 (*S*)	>49:1	64	*j*	4
12	**7**	(*R*)-**2**	10	55	84	96 (*S*)	>49:1	85	77	30[k]
13	**9**	(*R*)-**2**	1.5	45	86	74 (*S*)	>49:1	90	89	39[k]
14	**10**	(*R*)-**2**	2.5	56	86	99 (*S*)	>49:1	76	77	37[k]
15	**11**	(*R*)-**2**	3	48	94	87 (*S*)	>49:1	88	93	72
16	**12**	(*R*)-**2**	4	50	87	94 (*S*)	>49:1	82	93	100
17	**13**	(*R*)-**2**	1.5	38	80	58 (*S*)	>49:1	76	*j*	55
18	**14**	(*R*)-**2**	10	62	82	98 (*S*)	>49:1	81	*j*	18
19	**15**	(*R*)-**2**	6	46	94	78 (*S*)	>49:1	85	*j*	54
20	**19**	(*R*)-**2**	12	36	86	27 (*S*)	>49:1	74	*j*	4
21	**20**	(*R*)-**2**	10.5	34	88	20 (*S*)	>49:1	82	*j*	3
22	**21**	(*R*)-**2**	2	45	86	63 (*S*)	>49:1	87	76	14[k]
23	**22**	(*R*)-**2**	3	55	85	75 (*S*)	5:1	82	*j*	9
24	**21**	(*S*)-**1**	23	52	84	43 (*R*)	>49:1	80	38	3
25	**23**	(*R*)-**1**	1	97	*j*	51	2:1	*j*	*j*	1.4

[a] Reaction conditions were as follows: room temperature, 0.2 mmol of substrate, 0.01 mmol of ketone (*R*)-**1** or (*R*)-**2**, 0.5 mmol of Oxone, 1.55 mmol of $NaHCO_3$, solvents (for ketone (*R*)-**1**, 1.5 mL of CH_3CN, and 1 mL of aqueous Na_2·EDTA solution (4×10^{-4} M); for ketone (*R*)-**2**, 1 mL of DMM, 2 mL of CH_3CN, and 2 mL of aqueous Na_2·EDTA solution (4×10^{-4} M)). [b] (*R*)-**1** and (*R*)-**2**: 98% ee. Ketones (*R*)-**1** and (*R*)-**2** were recovered in over 80% yield by flash column chromatography and reused without loss of catalytic activity and chiral induction. [c] Conversion was determined by ^{1}H NMR of the crude reaction mixture after workup. In cases where the ee of epoxides has been determined, the conversion was cross-checked according to the equation: ee(olefin)/ee(epoxide) = $C/(1 - C)$. [d] Yield based on the conversion. [e] The ee value was determined by HPLC analysis of the corresponding allylic alcohol after deprotection except for substrate **7**. [f] The absolute configuration was determined by Mosher's method. [g] The ratio of *erythro*/*threo*-epoxides was determined by ^{1}H NMR. [h] The ee value was determined by HPLC (Chiralcel OD column). [i] The selectivity (*S*) was calculated by the equation $S = \ln[(1 - C)(1 - \text{ee})]/\ln[(1 - C)(1 + \text{ee})]$, where *C* is conversion and ee is percentage enantiomeric excess of the recovered substrate. [j] Not determined. [k] The selectivity (*S*) was the average of two runs.

large OTBDMS group blocks the other face of the double bond in conformer **B**, rendering the double bond inaccessible to dioxiranes. Therefore, only conformer **A** of the lowest free energy can be possibly epoxidized by dioxiranes approaching from the face opposite to the CCl_3 group. This explains the observed excellent diastereoselectivities in the kinetic resolution process with the *erythro*-epoxides as the major products.

Since the large OTBDMS group in conformer **A** blocks the approach of dioxiranes from the H-4 side of the double bond, the proposed spiro transition states[6,15] for epoxidation catalyzed by (*R*)-**1** or (*R*)-**2** could be simplified as the favored **C** and the disfavored **D** (Figure 3), in which chiral dioxiranes can only approach the double bond of the substrate from the phenyl side. In the favored TS-**C**, the phenyl ring of the (*R*)-enantiomer of the substrate is far away from the steric sensors, i.e., H-3 (Cl-3) or H-3′ (Cl-3′) of the (*R*)-dioxirane, and there is little steric or electrostatic interaction between the substrate and the dioxirane. In contrast, in the disfavored TS-**D**, the phenyl ring of the (*S*)-enantiomer of the substrate severely

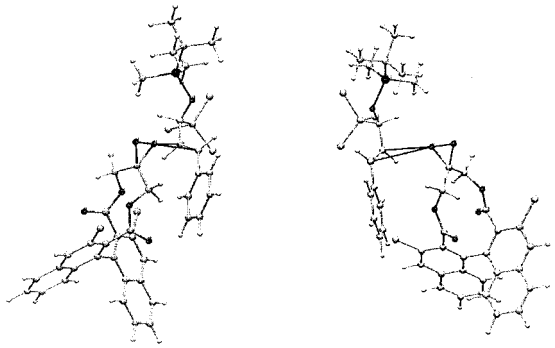


Figure 3. Transition states for kinetic resolution reactions catalyzed by ketone (*R*)-**2**.

(15) (a) Baumstark, A. L.; McCloskey, C. J. *Tetrahedron Lett.* **1987**, *28*, 3311. (b) Baumstark, A. L.; Vasquez, P. C. *J. Org. Chem.* **1988**, *53*, 3437. (c) Houk, K. N.; Liu, J.; DeMello, N. C.; Condroski, K. R. *J. Am. Chem. Soc.* **1997**, *119*, 10147. (d) Bach, R. D.; Andres, J. L.; Owensby, A. L.; Schlegel, H. B.; McDouall, J. J. W. *J. Am. Chem. Soc.* **1992**, *114*, 7207.

bumps into H-3 (Cl-3) or H-3′ (Cl-3′) of the (*R*)-dioxirane. Consequently, the (*S*)-enantiomer of the substrate would be less reactive than its corresponding (*R*)-form and is expected to be enriched in the recovered substrate.

Docking experiments using the MacroModel program[13] suggested that the steric sensors of dioxiranes can recognize the *para* and *meta* substituents on the phenyl rings of substrates. Thus, when the *para* substituent becomes bulkier, the steric interactions in the disfavored TS-**D** will be more severe, resulting in higher selectivity. Furthermore, electron-donating substituents intensify the electrostatic repulsion between the phenyl rings of substrates and the Cl atom or naphthyl ring of the dioxirane in the disfavored TS-**D**, which leads to higher selectivity. For the same substrate, ketone (*R*)-**2** gave much higher selectivity than ketone (*R*)-**1** because the presence of the Cl atom at the 3 and 3′ positions increases both steric interaction and electrostatic repulsion in the disfavored TS-**D**.

(4) Deprotection of the TBDMS Group on Substrates and Epoxides. To obtain the α-trichloromethyl allylic alcohols, we tested several reagents such as HF·pyridine,[16a] Bu_4NF,[16b] $BF_3{\cdot}Et_2O$,[16c] concentrated HCl,[16d] CF_3COOH,[16e] and AcOH[16b] for the deprotection of the TBDMS group on substrates **7** and **9**−**20**. While concentrated HCl, CF_3COOH, and AcOH were totally ineffective, Bu_4NF and $BF_3{\cdot}Et_2O$ removed the TBDMS group quickly but yielded some undesired side products due to their reactions with α-trichloromethyl allylic alcohols.[7d] HF·pyridine proved to be the most effective reagent, which generally gave clean α-trichloromethyl allylic alcohols in high yield (Table 3).[17]

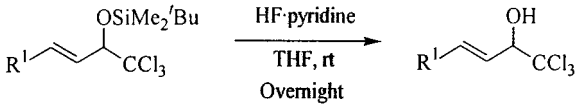
On the other hand, the TBDMS group on epoxides can be deprotected by Bu_4NF.[16b,18]

(5) Synthetic Applications of α-Trichloromethyl Allylic Alcohols. Two important transformations were investigated to demonstrate the synthetic utilities of chiral α-trichloromethyl allylic alcohols.

(a) Hydrogenation. Chiral allylic alcohol **3** was quantitatively converted to 4-phenyl-1,1,1-trichloro-2-butanol **24** without loss of enantioselectivity under high-pressure hydrogenation conditions (Scheme 1). The product **24** has been shown to be an important precursor for the preparation of chiral α-fluoro acids,[7d] α-hydroxy acids,[7e,f] or α-amino acids.[7e,f]

(b) One-Pot Rearrangement. As shown in Scheme 2, chiral allylic alcohol **3** with a 64% ee was coupled with thiocarbonyldiimidazole in CH_2Cl_2. The crude residue **25** after the aqueous workup was used directly in the rearrangement step without purification. The overall yield from **3** to the rearranged product **26** was 75% and the product also showed a 64% ee. The corresponding allylic thiol is a versatile intermediate in the synthesis of many sulfur-containing natural products.[7a,b]

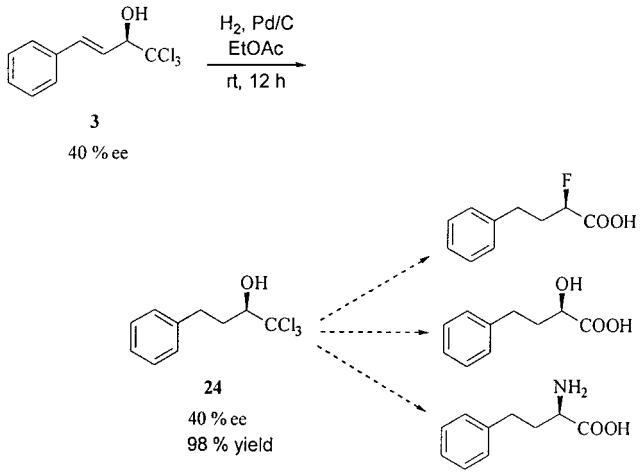
Table 3. Deprotection of α-Trichloromethyl Allylic TBDMS Ethers 7 and 9−20 to the Corresponding α-Trichloromethyl Allylic Alcohols



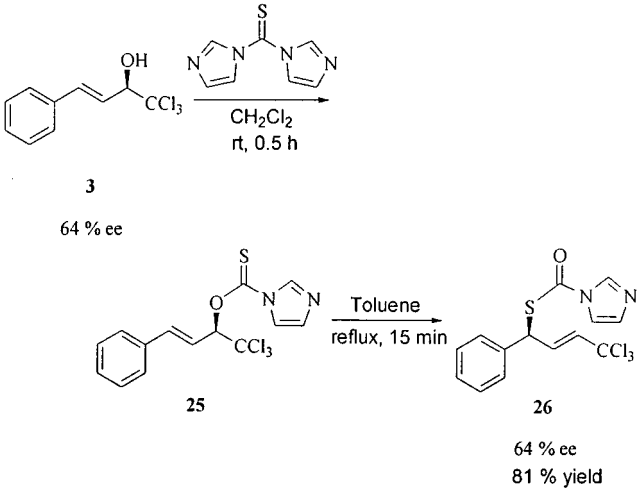
7 and 9–20 — 7c and 9c–20c

entry	substrate	product	yield (%)
1	**7**	**7c**	88
2	**9**	**9c**	91
3	**10**	**10c**	89
4	**11**	**11c**	90
5	**12**	**12c**	92
6	**13**	**13c**	86
7	**14**	**14c**	90
8	**15**	**15c**	91
9	**16**	**16c**	71
10	**17**	**17c**	85
11	**18**	**18c**	83
12	**19**	**19c**	82
13	**20**	**20c**	89

Scheme 1



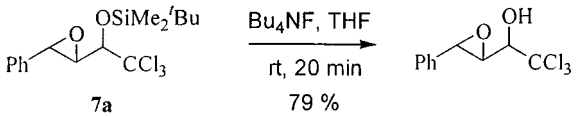
Scheme 2



(16) (a) Masamune, S.; Lu, L. D.-L.; Jackson, W. P.; Kaiho, T.; Toyoda, T. *J. Am. Chem. Soc.* **1982**, *104*, 5523. (b) Corey, E. J.; Venkateswarlu, A. *J. Am. Chem. Soc.* **1972**, *94*, 6190. (c) Kelly, D. R.; Roberts, S. M.; Newton, R. F. *Synth. Commun.* **1979**, *9*, 295. (d) Cunico, R. F.; Bedell, L. *J. Org. Chem.* **1980**, *45*, 4797. (e) Baker, R.; Cummings, W. J.; Hayes, J. F.; Kumar, A. *J. Chem. Soc., Chem. Commun.* **1986**, 1237.

(17) We also carried out the kinetic resolution of racemic α-trichloromethyl allylic alcohol **3** by Sharpless asymmetric epoxidation method, but low selectivity was obtained (S = 1.1). This is in line with the literature reports that Sharpless asymmetric epoxidation method is ineffective for resolutions of acyclic secondary allylic alcohols with a *tert*-butyl, CF_3, or difluoroethyl group at the α-position. See: (a) Schweiter, M. J.; Sharpless, K. B. *Tetrahedron Lett.* **1985**, *26*, 2543. (b) Kitano, Y.; Matsumoto, T.; Sato, F. *Tetrahedron* **1988**, *44*, 4073. (c) Hanzawa, Y.; Kawagoe, K. I.; Ito, M.; Kobayashi, Y. *Chem. Pharm. Bull.* **1987**, *35*, 1633.

(18) As an example, epoxide **7a** was deprotected to corresponding epoxy alcohol by Bu_4NF in 79% yield.



7a — 79 %

II. Resolutions of Other Acyclic Secondary Allylic TBDMS Ethers. To extend the scope of our kinetic resolution method, substrates **21**−**23**, with a *tert*-butyl, CF_3, or phenyl group at the α-position instead of a CCl_3 group, were subjected to the same kinetic resolution conditions. The results (Table 2, entries 22−25) revealed that the present method was also effective for resolution of substrates with a *tert*-butyl or CF_3 group at the α-position. In particular, *S* values of 14 and 9 were obtained in the resolutions of substrates **21** and **22**, respectively, with ketone (*R*)-**2** as the catalyst (entries 22 and 23). The smaller CF_3 group is less efficient than CCl_3 and *tert*-butyl groups in shielding one face of the double bond in the substrates, leading to lower diastereoselectivity and poorer resolution efficiency (entries 23 vs 22 and 12). Similar results were obtained for the phenyl group (entries 25 vs 24 and 1).

Conclusions

Kinetic resolution of acyclic secondary allylic alcohols and their derivatives catalyzed by chiral ketones has been investigated in some detail. It was found that the chiral ketone-catalyzed kinetic resolution method was effective for the acyclic secondary allylic silyl ethers with a CCl_3, *tert*-butyl, or CF_3 group at the α-position. A model was proposed to rationalize the observed enantioselectivities and diastereoselectivities in the kinetic resolution process based on steric and electrostatic interactions between the chiral dioxiranes and the racemic substrates. Since the TBDMS group on the substrates and epoxides can be easily removed,[16a,b] the present method provided a convenient access to both chiral secondary allylic alcohols with a CCl_3, *tert*-butyl, or CF_3 group at the α-position and chiral epoxy alcohols. With the ready availability of chiral α-trichloromethyl allylic alcohols by our method, future work will be directed at exploring their potential applications in organic synthesis.

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Supporting Information Available: Experimental details of kinetic resolution reactions; X-ray structural analysis of epoxides **12a**, **14a**, and **15a** containing tables of atomic coordinates, thermal parameters, bond lengths, and angles. This material is available free of charge via the Internet at http://pubs.acs.org.

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