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α-Functionalised Ketones as Promoters of Alkene Epoxidation by Oxone®

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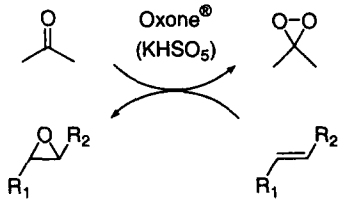
Abstract: Acceleration of Oxone® epoxidation of alkenes by several α-functionalised ketones, including α-amido ketones, is investigated. In general, competing decomposition by Baeyer-Villiger reaction prevents use of the ketones as efficient epoxidation promoters. However, a novel oxazolidinone-derived ketone provides epoxides with moderate enantioselectivity (up to 34% ee).

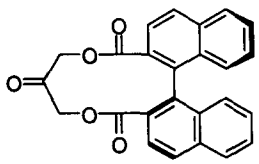
Keywords: Dioxiranes, epoxides, oxidation, ketones

Introduction

The catalysis of Oxone® epoxidation of alkenes by ketones (Scheme 1), *via* dioxirane intermediates,[1] is an area of considerable current interest, particularly in view of the possibility of asymmetric epoxidation when chiral ketones are used.[2-6] Early studies in this area employed a two-phase (CH_2Cl_2 / H_2O) solvent system for dioxirane generation which required careful pH control.[7] Enantioselectivities obtained using chiral ketones in this system were moderate, and conversions were often low.[2] An important contribution came from Yang and co-workers who introduced an experimentally simple, self-buffering CH_3CN / H_2O / $NaHCO_3$ system that allows the accelerating effect of ketones to be tested more easily.[8] Yang showed that electron withdrawing substituents α-to the carbonyl greatly increased the rate of reaction, and that α-acetoxyacetone was considerably more reactive than acetone itself.[3] This led to the development of chiral ketone **1** which, employed catalytically (10 mol%), afforded moderate-to-good enantioselectivities for epoxidation of a range of aromatic-substituted alkenes. Structural modifications allowed enantioselectivities to be further improved.[3] Amongst other attempts to develop chiral ketone catalysts, the best results to date have been described by Shi and co-workers[4] using the fructose-derived ketone **2**. Ketone **2** provides outstanding enantioselectivities for the epoxidation of a range of *trans*- and trisubstituted alkenes (for example, >95% ee for the epoxidation of *E*-stilbene). However, this ketone undergoes decomposition under the Yang reaction conditions, necessitating the use of three equivalents. Shi has since shown that lower amounts (30 mol%) of **2** can be used at higher pH (employing Na_2CO_3 in place of $NaHCO_3$).[4b]



Scheme 1



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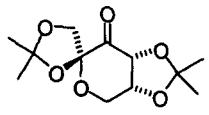

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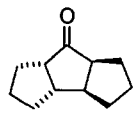
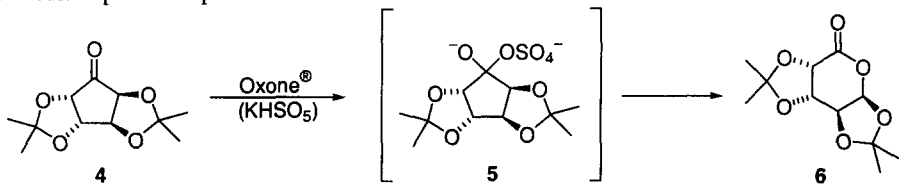
We have also been engaged in the design and synthesis of chiral ketones,[5] with the aim of developing stable catalysts that afford high enantioselectivities. We report here some of our early experiments in the testing of various α-functionalised ketones as epoxidation catalysts in the Yang *in situ* system.

Results and Discussion



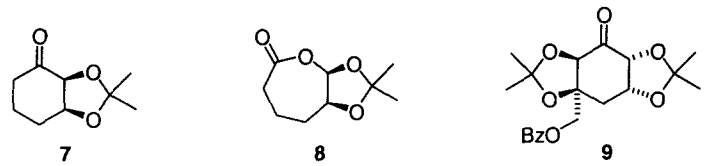
3

Contemporaneously with the work of Yang, our early experiments with various ketones led us also to realise that electronic activation of the ketone carbonyl would be essential for good catalytic activity. Thus, the known[9] C_2-symmetrical carbocycle **3** (1 eq or 10 eq) proved to be completely unreactive in the epoxidation of *E*-stilbene under the Yang conditions, and was recovered unchanged. In retrospect, this is not surprising since this hindered ketone is reported to be resistant to attack by nucleophiles.[9] With the aim of providing electronic activation whilst retaining the C_2-symmetrical motif, we prepared the novel acetal **4**.[5a] However, we found that **4** underwent rapid Baeyer-Villiger reaction to give the lactone **6** (Scheme 2), such that no epoxidation of *E*-stilbene was observed under the Yang conditions using 10 eq of **4**. The Baeyer-Villiger reaction likely proceeds *via* bond migration in the tetrahedral intermediate **5** that results from addition of $KHSO_5$ to the ketone carbonyl. While α-alkoxy functionality is known to promote the peracid-mediated Baeyer-Villiger reaction of ketones,[10] it was not clear to us at this time whether the ready ring expansion of **4** was due to the effect of the α-oxygenation, or due to inherent ring strain. We therefore prepared the simpler acetal **7**. Again, this proved to be a poor promoter: with 1 eq. of **7**, only 14% conversion of *E*-stilbene to the corresponding epoxide was observed after 24 hours, and **7** was converted completely into the lactone **8**. We concluded from this study that α-alkoxy substituents were inherently unsuitable for activating ketones as epoxidation promoters. Subsequent to these experiments, however, Shi reported that ketone **2** could function as an epoxidation promoter in the Yang system, and that its Baeyer-Villiger decomposition could be suppressed by increasing the pH.[4b] We have tested acetal **4** under Shi's modified higher pH conditions, but it is still totally ineffective, undergoing rapid Baeyer-Villiger decomposition. Recently, Shi has reported that the similar acetal system **9** is a stable and efficient catalyst,[4c] indicating that the balance between Baeyer-Villiger decomposition and dioxirane formation is a fine one, and difficult to predict at present.



4 5 6

Scheme 2

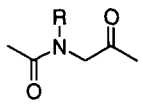


7 8 9

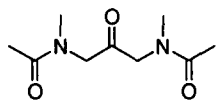
In considering alternative functionality that might activate the carbonyl group without promoting Baeyer-Villiger decomposition, we noted the stability of the Yang catalysts **1**, where the α-oxygenation is part of an ester. Presumably, resonance delocalisation of the O-lone pairs reduces their ability to assist Baeyer-Villiger bond migration. We were attracted to the idea that α-amide substituents might behave similarly to the corresponding esters, but with the additional attractive possibility that chirality could be introduced closer to the ketone by placing an extra substituent on nitrogen. As a prelude to the investigation of chiral α-amidoketones, a range of simple α-amidoketones **10-16** were synthesised and tested as catalysts for the epoxidation of *E*-stilbene. The results are shown in Table 1. Entry 1 shows that in the absence of a ketone, background

epoxidation of *E*-stilbene by Oxone® is low. Entries 2 and 3, included for comparison purposes, show that α-acetoxyacetone is an effective promoter. α-Acetamidoacetone **10** (10 eq) initially appeared to be almost as efficient (entry 4), giving high conversion after a similar time period. However, longer reaction times did not lead to significantly increased conversion (entry 5), suggesting catalyst decomposition. This was confirmed by TLC analysis when **10** was exposed to the reaction conditions in the absence of olefin. Small amounts of compounds tentatively assigned by ^{1}H NMR spectroscopic analysis as arising from Baeyer-Villiger reaction were obtained. Due to this competing decomposition, use of 1 equivalent of **10** resulted in low conversion (entry 6).

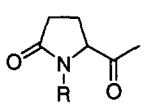
Despite these disappointing initial results, the effect of placing further substituents on nitrogen was examined. It was hoped that this might affect the Baeyer-Villiger – dioxirane competition, as well as eventually allowing easy access to chiral ketones. However, the *N*-methyl compound **11** (entries 7 and 8) and the *N*-acyl derivative **12** (entry 9) again did not promote epoxidation efficiently. In the case of **11**, analysis of the crude ^{1}H NMR spectrum again suggested that Baeyer-Villiger reaction was a problem, but we could see no sign of this for **12.** The *bis*-amido derivative **13** (entry 10) was also ineffective, although this may be partly due to its poor solubility in the reaction mixture.



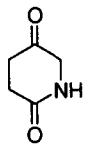
10 R = H
11 R = CH_3
12 R = $C(O)CH_3$



13



14 R = H
15 R = $C(O)CH_3$



16

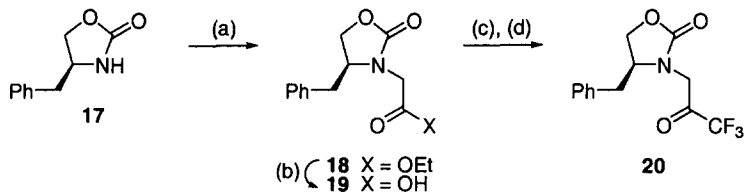
It seemed unlikely, therefore, that simple acyclic α-amidoketones would provide useful catalysts. In studying α-alkanoyloxyketones, however, Yang had noted that cyclic esters such as **1** were more reactive than their acyclic counterparts.[3] We therefore examined several cyclic amides, **14-16**. The methyl-ketones **14** and **15**, where the amide is constrained in a five-membered ring, were less effective than **10** (Table 1, entries 11-14). Again, ^{1}H NMR spectroscopic analysis suggested that **14** and **15** were undergoing Baeyer-Villiger decomposition. Ketone **16**, where the ketone carbonyl is part of a six-membered ring, was better (entries 15 and 16), and we could see no sign of Baeyer-Villiger decomposition. Overall, then, **16** appears to be the best promoter amongst the simple amides we have studied, with most of the others undergoing Baeyer-Villiger decomposition. While it should be noted that we have not tested any of these amidoketones under the Shi higher pH conditions, which may slow the decomposition pathway, they all seem to be less efficient promoters than α-acetoxyacetone. In view of the differing properties of structurally similar acetals **2**, **4**, **7** and **9**, however, it may be dangerous to extrapolate our observations with simple α-amidoketones to more complex systems.

Finally, we decided to investigate the effect of having the α-nitrogen as part of a carbamate functionality. From a synthetic viewpoint, it seemed that some of the easiest such compounds to synthesise would be those derived from readily available chiral oxazolidinones (*e.g.* **17**). Thus, alkylation of **17** with ethylbromoacetate provided **18**, which was converted to the corresponding acid **19** (Scheme 3). In view of the known high reactivity of trifluoroacetone as an epoxidation catalyst,[8] we decided to prepare the trifluoromethyl ketone **20**. This was easily obtained from **19** by heating the derived acid chloride with trifluoroacetic anhydride and pyridine according to the method of Zard.[11] Ketone **20** exists in a mixture with its hydrate which was used directly in the epoxidation reactions. In the event, ketone **20** suffered from the same Baeyer-Villiger problems as the simpler amides. However, using 3 equivalents of the ketone allowed good conversions to epoxide with moderate enantioselectivities (Table 2). When these results were first obtained, they were amongst the highest recorded for epoxidation of alkenes of this type by non-metal mediated processes, being comparable to the results of Yang using the ketone **1**. However, the selectivities since provided by the Shi ketones **2** and **9** are far superior. Nevertheless, the enantioselectivities afforded using **20** are promising for such a simple system.

Table 1 Epoxidation of *E*-stilbene by Oxone® and α-Amidoketones **10 – 16**[a]

Entry	Ketone	No. of equivalents	Time (hours)	Conversion[b] (%)
1	–	–	24	4
2	α-Acetoxyacetone	10	0.5	100
3	α-Acetoxyacetone	1	5	100
4	**10**	10	0.5	88
5	**10**	10	2	90
6	**10**	1	24	13
7	**11**	10	24	13
8	**11**	1	24	9
9	**12**	10	24	35
10	**13**	1	24	< 5
11	**14**	10	24	4
12	**14**	1	24	17
13	**15**	10	24	39
14	**15**	1	24	8
15	**16**	10	24	80
16	**16**	1	24	19

[a]*E*-Stilbene (0.1 mmol), $NaHCO_3$ (1.55 mmol), ketone, acetonitrile (1.5 ml), 0.4mM aq. Na_2EDTA (1 ml), Oxone® (1.0 mmol $KHSO_5$). [b]Conversion to epoxide, estimated by ^1H NMR spectroscopic integration.



Scheme 3

(a) NaH, $BrCH_2CO_2Et$, THF, 0°C to RT, 83%; (b) (i) NaOH, THF (ii) HCl, 98%; (c) $(COCl)_2$, toluene, 60°C, 100%; (d) $(CF_3CO)_2O$, pyridine, CH_2Cl_2, 79%.

Table 2 Alkene Epoxidation by Oxone® and Ketone **20**[a]

Alkene	Conversion	Epoxide yield[b]	Epoxide ee (%)[c]
E-Stilbene	75	69	25 (*R*, *R*)
E-2-Methylstilbene	65	52	31 (*R*, *R*)
E-2-Phenylstilbene	33	26	33 (*R*)
1-Phenylcyclohexene	100	67	34 (*R*, *R*)
Styrene	64	18	< 5
E-Methylcinnamate	0	0	–

[a]Alkene (0.1 mmol), Oxone® (1.0 mmol $KHSO_5$), $NaHCO_3$ (1.55 mmol), ketone **20** (0.3 mmol), CH_3CN (1.5 ml), 0.4mM aqueous Na_2EDTA (1 ml), 24 hours, R.T. [b]Isolated yield of pure epoxide. [c]Measured by ^1H NMR in the presence of chiral shift reagent (see ref. 3a). Absolute configuration in parentheses.

Conclusions

We have examined several types of α-functionalised ketone as promoters of the Oxone® epoxidation of alkenes. The hindered ketone **3** was unreactive, suggesting that electronic activation was necessary. The tricyclic acetal **4** underwent rapid decomposition by Baeyer-Villiger reaction, even at higher pH. Comparison to literature results on carbohydrate derived acetals[4] demonstrates that dioxirane formation and Baeyer-Villiger reaction are finely balanced.

We have investigated a range of simple α-amidoketones as epoxidation promoters in the Yang system and have found them to be less effective than α-acetoxyacetone. Baeyer-Villiger decomposition is again a problem. However, given the subtle structural dependency revealed by the acetal systems, and the fact that we have not tested these compounds under the Shi higher pH conditions, it is possible that more functionalised α-amido systems might prove useful. We prepared the novel chiral oxazolidinone **20**; while Baeyer-Villiger reaction is again a problem, **20** affords enantioselectivities that are respectable for such a simple system.

Experimental

General Details

NMR spectra were recorded on Jeol GX 270, Jeol EX 270, Jeol EX 400, Bruker AM 400 or Bruker DRX 500 spectrometers. *J* values are measured in Hertz and are quoted to the nearest 0.5 Hz. Multiplicities in ^{13}C spectra were determined by DEPT experiments. Infra red spectra were recorded on a Perkin-Elmer 1605 FT-IR spectrometer. Microanalyses were performed in the School of Chemistry, University of Bath, and the Department of Chemistry, University of Nottingham. Melting points were recorded on a Kofler hot stage apparatus and are uncorrected. Optical rotations were recorded on a JASCO DIP-310 spectrometer. Flash column chromatography was performed using Matrex silica Si. Where appropriate the silica was neutralised by flushing it once with a 1% solution of triethylamine. Petrol refers to light petroleum b.p. 40-60°C. Thin layer chromatography was performed on Merck silica gel 60 F_{254} precoated glass tlc plates, visualised under UV and developing with basic permanganate solution, iodine or ceric ammonium molybdate. Tetrahydrofuran and diethylether (referred to throughout as ether) were distilled from sodium benzophenone ketyl. Benzene and toluene were distilled from sodium. Light petroleum b.p. 40-60°C (referred to throughout as petrol) was distilled from calcium sulfate. Methanol was distilled from Mg/I_2. Triethylamine, pyridine, dichloromethane and acetonitrile were distilled from calcium hydride. Other reagents were either used as supplied or purified using standard techniques unless otherwise stated.

Preparation of Ketones

Ketones **3**,[9] **4**,[5a] **10**,[12] **11**,[13] **12**,[10] **13**,[14] **14**,[15] **15**,[16] **16**[17] are all literature compounds.

(3aR,7aR*)-2,2-Dimethyl-tetrahydrobenzo[1,3]dioxol-4-one* **7**

To a solution of 2,3-dihydroxycyclohexanone[18] (0.47 g, 3.6 mmol) in acetone (20 ml) was added *p*-toluenesulfonic acid (10 mg, 0.06 mmol). The mixture was stirred at room temperature for 3 days, and saturated aqueous $NaHCO_3$ solution (2 ml) added. After concentration to *ca.* 10 ml the mixture was extracted into ethyl acetate (4 x 50 ml), dried over $MgSO_4$, filtered and the solvent removed under reduced pressure. Flash column chromatography (ether) gave the *acetonide* **7** (308 mg, 50%) as a colourless solid, mp 77-78°C; ν_{max} /cm^{-1} 2938, 1716, 1374, 1236, 1059; δ_H (400 MHz, $CDCl_3$) 4.61 (1H, m, 7a-H), 4.28 (1H, d, *J*5.5, 3a-H), 2.54-2.47 (1H, m, 5-H), 2.35-2.26 (1H, m, 5-H), 2.22-1.88 (3H, m, 6-H and 7-H), 1.44 (3H, s, CH_3), 1.39 (3H, s, CH_3); δ_C (67.9 MHz, $CDCl_3$) 208.5 (C), 109.7 (C), 79.3 (CH), 77.1 (CH), 40.1 (CH_2), 27.0 (CH_3), 26.9 (CH_2), 26.0 (CH_3), 20.3 (CH_2); *m/z* (EI) 170 (M^+, 16%); Found: M^+, 170.0943. $C_9H_{14}O_3$ requires: M, 170.0943.

(4S)-(+)-(4-Benzyl-2-oxo-oxazolidine-3-yl)-acetic acid ethyl ester **18**

To a solution of 4-benzyl-oxazolidin-2-one **17** (3.5 g, 19.7 mmol) in tetrahydrofuran (50 ml) at 0°C was added sodium hydride (500 mg, 20.8 mmol) and ethyl bromoacetate (4 ml, 36.0 mmol). The resulting suspension was stirred for 8.5 hours, allowing to warm to room temperature. Further ethyl bromoacetate (1 ml, 9.0 mmol) was added and the mixture stirred for a further 3 hours. Saturated aqueous ammonium chloride (50 ml) was added, followed by water (25 ml), and the mixture extracted into ether (3 x 100 ml). The combined organics were dried over $MgSO_4$, filtered, and the solvent removed under reduced pressure. Flash column chromatography (66% ether in petrol) gave the *ester* **18** (4.29 g, 83%) as a colourless oil, $[\alpha]_D^{20}$ +19.0 (*c* 0.496, EtOH); ν_{max} /cm^{-1} 2983, 2933, 1746, 1432, 1209, 1028; δ_H (270 MHz, $CDCl_3$) 7.36-7.14 (5H, m, Ar-H), 4.36-4.14 (5H, m, 4-H, 5-H, 4'-CH_2, 1'-H), 4.05-4.01 (1H, m, 5-H), 3.68 (1H, d, *J*18.0, 1'-H), 3.03 (1H, dd, *J*13.5, 5.5, 1''-H), 2.76 (1H, dd, *J*13.5, 8.0, 1''-H), 1.27 (3H, t, *J*7.1, 5'-H); δ_C (67.9 MHz, $CDCl_3$) 168.4 (C), 158.4 (C), 135.3 (C), 129.9 (2 x CH), 127.2 (CH), 67.5 (CH_2), 61.5 (CH_2), 56.2 (CH), 43.8 (CH_2), 38.7 (CH_2), 14.1 (CH_3); *m/z* (EI) 263 (M^+, 3%), 219 (M^+-CO_2, 15), 190 (M^+-CO_2Et, 15), 172 (M^+-Bn, 100); Found: M^+, 263.1159. $C_{14}H_{17}O_4N$ requires: M, 263.1158.

(4S)-(+)-(4-Benzyl-2-oxo-oxazolidine-3-yl)-acetic acid **19**

To a solution of the ester **18** (4.25 g, 16.1 mmol) in tetrahydrofuran (50 ml) was added 2M NaOH (30 ml). After stirring at room temperature for 15 minutes the solution was acidified with 2M HCl (35 ml), and extracted into ethyl acetate (3 x 100 ml). The combined organics were dried over $MgSO_4$, filtered, and the solvent removed under reduced pressure to give the *acid* **19** (3.55 g, 98%) as a colourless solid, m.p. 131-136°C, $[\alpha]_D^{19}$ +55.5 (*c* 1.14, EtOH). ν_{max} /cm^{-1} 2921, 2605, 1748, 1691, 1477, 1456, 1395, 1233, 1118, 1021, 764, 697; δ_H (270 MHz, $CDCl_3$) 9.47 (1H, bs, CO_2H), 7.37-7.15 (5H, m, Ar-H), 4.37-4.11 (3H, m, 4-H, 5-H, 1'-H), 4.07 (1H, dd, *J*8.0, 6.0, 5-H), 3.76 (1H, d, *J*18.5, 1'-H), 3.07 (1H, dd, *J*13.5, 5.1, 1''-H), 2.78 (1H, dd, *J*13.5, 8.0, 1''-H); δ_C (67.9 MHz, $CDCl_3$) 172.6 (C), 158.9 (C), 135.1 (C), 129.1 (CH), 128.9 (CH), 127.4 (CH), 67.8 (CH_2), 56.5 (CH), 43.6 (CH_2), 38.7 (CH_2); *m/z* (EI) 235 (M^+, 8%), 144 (M-Bn, 100%); Found: M^+, 235.0845. $C_{16}H_{26}O_2$ requires: M, 235.0844.

(4S)-4-Benzyl-3-(3,3,3-trifluoro-2-oxo-propyl)-oxazolidin-2-one **20** and its hydrate

To a suspension of the acid **18** (300 mg, 1.35 mmol) in toluene (20 ml) at room temperature was added oxalyl chloride (335 µl, 3.84 mmol). The suspension was heated to 60°C for 2.5 hours, over which time the acid dissolved. Removal of the solvent under reduced pressure gave crude acid chloride (324 mg, 100%) as a pale solid which was used directly in the subsequent reaction. Data for the acid chloride: ν_{max} /cm^{-1} 2919, 1799, 1749, 1429, 1256, 1182, 1105, 1029, 961, 825, 740, 702, 668; δ_H (270 MHz, $CDCl_3$) 7.39-7.15 (5H, m, Ar-H), 4.57 (1H, d, *J*19.0, 1'-H), 4.40 (1H, t, *J*8.0, 5-H), 4.24 (1H, m, 4-H), 4.08 (1H, dd, *J*8.0, 6.5, 5-H), 4.01 (1H, d, *J*19.0, 1'-H), 3.00 (1H, dd, *J*14.0, 6.5, 1''-H), 2.84 (1H, dd, *J*14.0, 7.0, 1''-H); δ_C (67.9 MHz, $CDCl_3$) 170.8 (C), 157.8 (C), 134.8 (C), 129.0 (CH), 128.7 (CH), 127.6 (CH), 67.8 (CH_2), 56.1 (CH), 53.5 (CH_2), 39.1 (CH_2).

To a solution of the acid chloride (2.40 g, 9.93 mmol) in dichloromethane (100 ml) were added trifluoroacetic anhydride (8.3 ml, 60 mmol) and pyridine (6.5 ml, 80.4 mmol). After stirring for 90 minutes water (15 ml) was added, the reaction mixture separated and the aqueous phase extracted into dichloromethane (3 x 50 ml). The combined organics were dried over $MgSO_4$, filtered, and the solvent removed under reduced pressure. Flash column chromatography (ether) gave a mixture of the *ketone* **20** and the corresponding hydrate (2.35 g, 79%, ketone : hydrate = 21:79) as a colourless solid, ν_{max}/cm^{-1} 3354, 2919, 1723, 1479, 1446, 1254, 1176, 1145, 1089, 1020, 768, 748, 702; δ_H (270 MHz, $CDCl_3$) 7.38-7.15 ($5H_{ketone}$ and $5H_{hydrate}$, Ar-H), 5.08 ($2H_{hydrate}$, O*H*), 4.55 ($1H_{ketone}$, d, *J* 20.0, 1'-H), 4.47 ($1H_{ketone}$, t, *J*8.0, 5-H), 4.34 ($1H_{hydrate}$, t, *J*8.0, 5-H), 4.29-4.09 ($2H_{ketone}$ and $2H_{hydrate}$, m, 4-H, 5-H), 4.00 ($1H_{ketone}$, d, *J*20.0, 1'-H), 3.73 ($1H_{hydrate}$, d, *J*15.0, 1'-H), 3.56 ($1H_{hydrate}$, d, *J*15.0, 1'-H), 3.20 ($1H_{hydrate}$, dd, *J*13.5, 4.0, 1''-H), 2.93 ($1H_{ketone}$, dd, *J*14.0, 7.0, 1''-H), 2.85 ($1H_{ketone}$, dd, *J*14.0, 7.0, 1''-H), 2.72 ($1H_{hydrate}$, dd, *J*13.5, 9.0, 1''-H); δ_C (67.9 MHz, $CDCl_3$) 161.6 ($C_{hydrate}$), 135.0 (C_{ketone}), 134.7 ($C_{hydrate}$), 129.2 (CH_{ketone}), 129.1 ($CH_{hydrate}$), 129.0 ($CH_{hydrate}$), 128.7 (CH_{ketone}), 127.6 (CH_{ketone}), 127.4 ($CH_{hydrate}$), 127.4 ($CF_{3hydrate}$, $^1J_{CF}$130), 93.6 (*C*-CF_3, $^2J_{CF}$32), 68.8 ($CH_{2hydrate}$), 68.0 ($CH_{2hydrate}$), 58.4 ($CH_{hydrate}$),

56.2 (CH_{ketone}), 47.3 ($CH_{2ketone}$), 45.6 ($CH_{2hydrate}$), 39.4 ($CH_{2ketone}$), 38.4 ($CH_{2hydrate}$); *m/z* (EI) 306 ($MH_{hydrate}^+$, 97%), 288 (MH_{ketone}^+, 100); Found: $MH_{hydrate}^+$, 306.0924. $C_{13}H_{15}O_4NF_3$ requires: M, 306.0953. Found: MH_{ketone}^+, 288.0848. $C_{13}H_{13}O_3NF_3$ requires: M, 288.0867.
(Neither C=O nor CF_3 peaks resolved in ^{13}C spectrum for ketone).

General Epoxidation Procedures
(a) One-phase epoxidation system - Yang[8]
To a solution of ketone and alkene (0.1 mmol) in acetonitrile (1.5 ml) was added aqueous Na_2EDTA solution (0.4 mM, 1 ml) followed by a mixture of Oxone® (307 mg, 1.0 mmol $KHSO_5$) and $NaHCO_3$ (130 mg, 1.55 mmol) in portions over 30 minutes. After the reaction was seen to be complete by TLC or after 24 hours, water (10 ml) was added, and the reaction mixture extracted into ether (3 x 25 ml). The combined organics were dried over $MgSO_4$, filtered, and the solvent removed under reduced pressure. Flash column chromatography (10% ether - petrol) on silica previously washed with 1% Et_3N in the eluent afforded the epoxide.

(b) One-phase epoxidation system - Shi pH 10[4b]
To a solution of alkene (0.1 mmol) and ketone in CH_3CN (1.5 ml) was added tetrabutylammonium hydrogensulfate (2 mg, 5.9 μmol) and $Na_2B_4O_7$ (0.05M in 0.4mM aqueous Na_2EDTA, 1 ml). After cooling to 0°C, a solution of Oxone® (85 mg, 0.138 mmol $KHSO_5$) in 0.4mM aqueous Na_2EDTA (0.65 ml) and a solution of K_2CO_3 (80 mg, 0.58 mmol) in water (0.65 ml) were added simultaneously by syringe pump over 90 minutes. The reaction was vigorously stirred until TLC indicated consumption of either alkene or ketone. Water (5 ml) was added and the mixture extracted into ether (3 x 10 ml). The combined organics were dried over $MgSO_4$, filtered, and the solvent removed. Flash column chromatography (10% ether - petrol) on silica previously washed with 1% Et_3N in the eluent afforded the epoxide.

Determination of epoxide e.e.
Epoxide e.e. was calculated by ^1H NMR analysis of the purified epoxide in the presence of $Eu(hfc)_3$ as a chiral shift reagent according to the procedure of Yang.[3a] The major enantiomer obtained was assigned by comparison to data obtained by the groups of Yang[3a] or Shi.[4b]

Ketone Decomposition Products
Lactone **6** has been reported previously.[5a]

2,2-Dimethyl-tetrahydro-[1,3]dioxolo[4,5-b]oxepin-5-one **8**
The ketone **7**, when tested as a promoter in the Yang, one phase epoxidation system, is converted to the *lactone* **8**, isolated by flash column chromatography (10 mg, 56%) as a colourless solid, mp 117-120°C; ν_{max} /cm^{-1} 2967, 1740; δ_H (270 MHz, $CDCl_3$) 5.84 (1H, d, *J*3.5, 3a-H), 4.30 (1H, m, 8a-H), 2.67 (1H, dd, *J*14.0, 10.0, 6-H), 2.51-2.38 (1H, m, 6-H), 2.25-2.17 (1H, m, 7-H or 8-H), 2.04-1.93 (1H, m, 7-H or 8-H), 1.95-1.62 (2H, m, 7-H or 8-H), 1.57 (3H, s, CH_3), 1.41 (3H, s, CH_3); δ_C (67.9 MHz, $CDCl_3$) 170.1 (C), 112.6 (C), 110.1 (CH), 78.6 (CH), 32.4 (CH_2), 27.8 (CH_3), 26.5 (CH_2), 26.2 (CH_3), 16.0 (CH_2); *m/z* (EI) 186 (M^+, 13%), 10 (M-acetone, 100); Found: M^+, 186.0892. $C_9H_{14}O_4$ requires: M, 186.0892.

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