Design of Efficient Ketone Catalysts for Epoxidation by Using the Field Effect

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Received June 29, 1998

By using the field effect (through-space charge-dipole or dipole−dipole interactions), efficient ketone catalysts **7** and **10** were developed for in situ epoxidation of olefins with Oxone. With either ketone **7** (10−20 mol %) or **10** (5−10 mol %) as catalyst, epoxidation of various olefins (2 mmol scale) at room temperature with 1.5 equiv of Oxone was complete in a short period of time with excellent isolated yields of epoxides (80−97%) and good ketone recovery (~80%). Furthermore, the in situ epoxidation of olefins can be performed on a large scale (20−100 mmol) directly with 5 mol % of commercially available tetrahydrothiopyran-4-one, which is oxidized by Oxone to ketone **10** during the epoxidation reactions.

Introduction

Dioxiranes[1] are powerful oxidants for epoxidation of olefins under mild and neutral reaction conditions.[2] The most commonly used dioxiranes, i.e., dimethyldioxirane and methyl(trifluoromethyl)dioxirane, can be obtained by distillation.[3] For preparative epoxidation, an operationally simple method is to generate dioxiranes in situ from ketones and Oxone.[4−7] Compared with acetone, 1,1,1-trifluoroacetone is much more reactive for in situ epoxidation though 10-fold excess is usually used.[6] Thus, there is a need to search for highly efficient ketone catalysts that are readily available, especially for asymmetric epoxidation.[8−12] Recently, three classes of ketones, 4-oxopiperidinium salts,[7] α-fluoro ketones,[12] and α,α′-bis-(ammonium) ketone,[13] have been reported by Denmark and co-workers for epoxidation with 10 mol % catalyst loading. However, those ketone catalysts require 10 equiv of Oxone to complete the epoxidation reactions. Here, we report that by using the field effect[14] (through-space charge-dipole or dipole−dipole interactions) efficient ketone catalysts are developed for in situ epoxidation with 5−20 mol % catalyst loading and 1.5 equiv of Oxone.

Results and Discussion

Efficient ketone catalysts for in situ epoxidation should have the following features given the possible reaction pathways shown in Scheme 1.[4,7] (1) Ketones are activated toward nucleophilic addition of Oxone to form dioxiranes; (2) the nonproductive decomposition of Oxone mediated by dioxiranes is minimized; and (3) ketones are stable under the neutral oxidation conditions.

A recent report of using the electrostatic field effect to design a new class of enzyme inhibitors containing

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(3) For example of the isolation of dimethyldioxirane by a distillation method, see: (a) Murray, R. W.; Jeyaraman, R. *J. Org. Chem.* **1985**, *50*, 2847. For examples of the isolation of methy(trifluoromethyl)-ldioxirane by a distillation method, see: (b) Mello, R.; Fiorentino, M.; Fusco, C.; Curci, R. *J. Am. Chem. Soc.* **1989**, *111*, 6749. (c) Adam, W.; Gonzalez-Nunez, M. E.; Mello, R.; Curci, R. *J. Am. Chem. Soc.* **1991**, *113*, 7654.

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10.1021/jo981270r CCC: $15.00
Published on Web 10/29/1998

Scheme 1

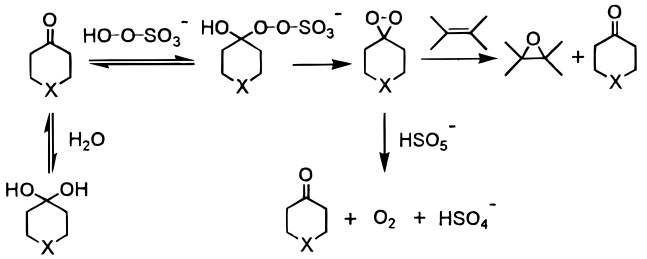
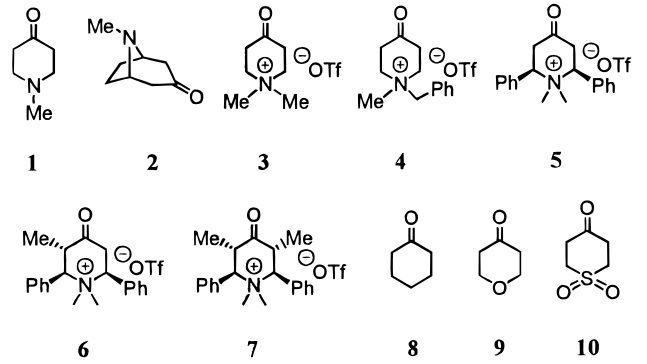


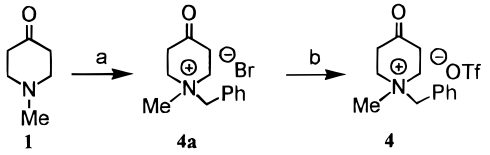
Chart 1



1 **2** **3** **4** **5**

6 **7** **8** **9** **10**

Scheme 2. Synthesis of Ketone 4[a]



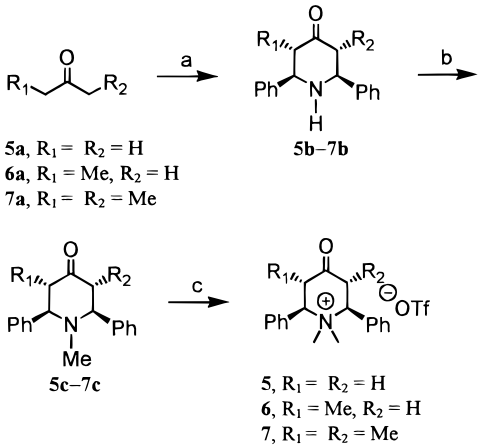
1 **4a** **4**

[a] Reagents and conditions: (a) benzyl bromide, CH_3CN, rt; (b) silver triflate, CH_3CN/H_2O, rt.

4-heterocyclohexanone rings[15] has brought our attention to the possibility of applying the concept in designing new ketone catalysts for epoxidation. Thus, a series of 4-heterocyclohexanones **1**−**10** (Chart 1) was chosen to probe the importance of the field effect of the heterosubstituents to the catalytic activities of those ketones. Ketone **4** was synthesized in two steps: reaction of *N*-methylpiperidone **1** with benzyl bromide and exchange of bromide ion of ketone **4a** by triflate ion (Scheme 2). Ketones **5**−**7** were prepared by using the Mannich reaction[16] followed by the two methylation steps (Scheme 3). Ketone **10** was prepared from the commercially available tetrahydrothiopyran-4-one by oxidation with Oxone in 75% yield.[17]

Ketones with positively charged ammonium groups as the heterosubstituents are highly electrophilic because the unfavorable through-space charge-dipole repulsion (the field effect) between the ammonium groups and the carbonyl group can be dissipated by rapid addition of nucleophiles such as HSO_5^- or water. As shown in Table

Scheme 3[a]



[a] Reagents and conditions: (a) benzaldehyde, NH_4OAc, 95% EtOH, reflux; (b) MeI, K_2CO_3, acetone, reflux; (c) methyl triflate, CH_2Cl_2, 0 °C to rt.

1, under our previously reported in situ conditions,[6] ketones **1**−**3** (entries 1−3) were highly active in catalyzing decomposition of Oxone (20 equiv of Oxone were consumed within 5 min), and only ketone **3** gave some *trans*-stilbene epoxide product.[7,18] This could be understood as that, at neutral pH, the in situ generated dioxiranes bearing the positively charged ammonium groups[19] would attract HSO_5^- anion and thereby decompose Oxone rapidly. We expect the nonproductive decomposition of Oxone to be slowed if the positive charges are shielded by bulky groups such as phenyl rings. Indeed, ketones **4**−**7** were found to give slower Oxone decomposition and higher epoxide yield (entries 4−7, Table 1). Ketones **5** and **6** were unstable under the reaction conditions and self-decomposed to unsaturated ketones **11**[20] and **12**,[21] respectively. In contrast, the two equatorial methyl groups of ketone **7**[22] apparently increased its stability by preventing the anti elimination of the ammonium group. Among this series of ammonium ketones, ketone **7** has the best catalytic activity. As revealed in Table 1, ketones **3**−**7** showed moderate to high hydration (K = 0.1−13.5 M^{-1}), yet no general correlation between the activities of ketones in catalyzing epoxidation and their hydration equilibrium constants was found.

Another way to enhance the electrophilicity of 4-heterocyclohexanones is to introduce the unfavorable dipole−dipole repulsion (the field effect) between the neutral heterosubstituents and the carbonyl group. Indeed, the hydration equilibrium constants[15,23] and rates of epoxidation increased dramatically as the field effect of the heterosubstituents increased (from cyclohexanone **8** to tetrahydropyran-4-one **9** to sulfone ketone **10**; entries

(15) Conroy, J. L.; Sanders, T. C.; Seto, C. T. *J. Am. Chem. Soc.* **1997**, *119*, 4285. The experimental results suggested that the apparent equilibrium constants for addition of thiol to 4-heterocyclohexanones gave a linear correlation with the field substituent constants *F* of the heterosubstituents at the 1-position of the ring.

(16) Preparations of **5b**−**7b** were carried out according to the literature procedure: Ravindran, T.; Jeyaraman, R. *J. Org. Chem.* **1991**, *56*, 4833. Preparations of **5c**−**7c** were carried out according to the literature procedure: Balasubramanian, M.; Padma, N. *Tetrahedron* **1963**, *19*, 2135.

(17) Casy, G.; Sutherland, A. G.; Taylor, R. J. K.; Urben, P. G. *Synthesis* **1989**, 767.

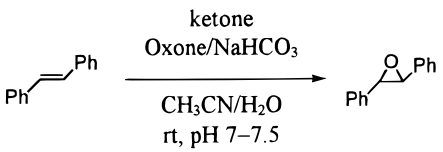
(18) Montgomery, R. E. *J. Am. Chem. Soc.* **1974**, *96*, 7820.

(19) The pK_a value of ketone **1** is 7.9. (Geneste, P.; Hugon, I.; Reminiac, C.; Lamaty, G.; Roque, J. P. *Bull. Soc. Chim. Fr.* **1976**, 845.) As we previously reported, the pH of the reaction was maintained at 7.0−7.5 by Oxone and sodium bicarbonate (see ref 6); the amino group of ketone **1** would be mostly protonated. The ratio of protonated form to ketone **1** would be 2.5:1 to 7.9:1 at pH 7.5−7.0. Similar to ketone **1**, ketone **2** would also be protonated during the reaction.

(20) The characterization data of **11** were consistent with those reported in the literature. Rampal, J. B.; Satyamurthy, N.; Bowen, J. M.; Purdie, N.; Berlin, K. D. *J. Am. Chem. Soc.* **1981**, *103*, 7602.

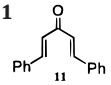
(21) The characterization data of **12** were consistent with those reported in the literature. Ramalingam, K.; Berlin, K. D. *J. Org. Chem.* **1979**, *44*, 477.

Table 1. Hydration Equilibrium Constants[a] for Ketones 1−10 and Their Activities in Catalyzing in Situ Epoxidation of *trans*-Stilbene with a 1:1 Ketone/Substrate Ratio[b]

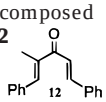


entry	ketone	K (M^{-1})	reaction time (min)[c]	epoxide yield[d] (%)	ketone recovery (%)
1[e]	**1**	0.28	*f*	*f*	*g*
2[e]	**2**	*h*	*f*	*f*	*g*
3[e]	**3**	13.5	*i*	*i*	*g*
4	**4**	12.1	45	95	*g*
5[j]	**5**	13.5	120	92	*k*
6[j]	**6**	1.8	120	87	*l*
7	**7**	0.1	15	94	82[m,n]
8	**8**	0.04[o]	*p*	*p*	*q*
9	**9**	0.23	30	93	*q*
10	**10**	11.1	2−3	97	96[m,r]

[a] $K = K_{eq}[H_2O] = 55.5K_{eq}$ (at 20 °C); K_{eq} = [hydrate]/[[ketone]-[H_2O](1/2.5)]. For determination of hydration equilibrium constants for ketones **1**, **3**−**7**, **9**, and **10**, see the Supporting Information. [b] Unless otherwise stated, reaction conditions were as follows: room temperature, 0.1 mmol of ketone, 0.1 mmol of *trans*-stilbene, 0.5 mmol of Oxone, 1.55 mmol of $NaHCO_3$, 1.5 mL of CH_3CN, 1.0 mL of aqueous Na_2·EDTA solution (4×10^{-4} M). [c] Time for epoxidation to complete as shown by TLC. [d] Isolated yield after flash column chromatography. [e] 2.0 mmol of Oxone and 6.2 mmol of $NaHCO_3$ were used. [f] No epoxidation occurred, but Oxone was consumed within 5 min. [g] Not attempted as the ketone was soluble in water. [h] Not determined. [i] After Oxone was consumed within 5 min, the reaction was worked up as usual. From the ^{1}H NMR, the ratio of *trans*-stilbene to its epoxide was found to be 1:6.6. [j] 1.0 mmol of Oxone and 3.1 mmol of $NaHCO_3$ were used. [k] The decomposed product was found to be the unsaturated ketone **11**



(85% yield). [l] The decomposed product was found to be the unsaturated ketone **12**



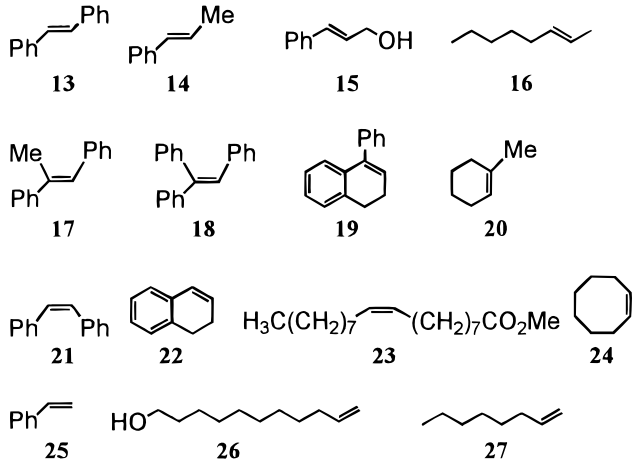
(69% yield). [m] The reaction mixture was diluted with CH_2Cl_2, dried over $MgSO_4$, filtered, and evaporated to dryness. [n] After the workup, ketone **7** was precipitated with hexane as a white solid. [o] Data taken from ref 15. [p] After 12 h, the reaction was worked up as usual. From the ^{1}H NMR spectrum, the ratio of *trans*-stilbene to its epoxide was found to be 1:0.5. [q] After the usual workup, the ^{1}H NMR spectrum of the reaction mixture showed that the ketone was stable. [r] Ketone was recovered by flash column chromatography.

8−10, Table 1). In addition, unlike those ammonium ketones, much slower decomposition of Oxone was observed with neutral ketones **8**−**10**. Using a 1:1 ratio of ketone/substrate, epoxidation of *trans*-stilbene catalyzed by ketone **10** was complete in 2−3 min. This experimental result indicates that ketone **10** has the highest catalytic activity among those ketones screened.

To further probe the catalytic efficiency of ketones, epoxidation of 15 olefins **13**−**27** was examined on a 2 mmol scale with either ketone **7** (10−20 mol %) or **10** (5−10 mol %) as catalyst. As shown in Table 2, all of the epoxidation reactions were complete with only 1.5 equiv of Oxone in a short period of time (0.5−8 h). The epoxides can be isolated in excellent yields (80−97%), and ketones **7** and **10** can be recovered in good yields (∼80%) by precipitation with hexane and by flash column chromatography, respectively. Compared with the previous reports of employing either 4-oxopiperidinium salts or α,α′-bis(ammonium) ketone as catalysts (10 mol %),[24] epoxidation reactions of substrates **14**, **15**, and **27** catalyzed by ketone **10** (5 mol %) were complete in a much

Table 2. Epoxidation of Olefins with Ketones 7 (10−20 mol %) and 10 (5−10 mol %) as Catalysts[a]

substrates:



entry	substrate	ketone[b]	cat. loading (mol %)	reaction time[c] (h)	epoxide yield[d] (%)
1	**13**	**7**	20	1.5	97[10c]
2	**13**	**10**	5	5	95
3	**14**	**7**	10	3	85[10c]
4	**14**	**10**	5	4.5	87
5	**15**	**7**	20	0.5	96[26]
6	**15**	**10**	5	1.5	95
7	**16**	**7**	10	8	87[27]
8	**16**	**10**	5	1.5	81
9	**17**	**7**	20	2.5	95[10c]
10	**17**	**10**	5	4	97
11	**18**	**7**	20	4.5	96[10c]
12	**18**	**10**	10	6	97
13	**19**	**7**	20	2	92[10c]
14	**19**	**10**	5	2.5	94
15	**20**	**7**	10	0.75	85[10c]
16	**20**	**10**	5	0.5	83
17	**21**	**7**	20	3	91[28]
18	**21**	**10**	5	4	95
19	**22**	**7**	20	1.5	83[10c]
20	**22**	**10**	5	2.5	85
21	**23**	**7**	20	2	94[29]
22	**23**	**10**	5	3	96
23	**24**	**7**	10	1.5	95[29]
24	**24**	**10**	5	0.5	96
25	**25**	**7**	10	7	82[30]
26	**25**	**10**	5	4.5	80
27	**26**	**7**	20	2.5	94[31]
28	**26**	**10**	5	3.5	95
29	**27**	**7**	10	8	90[27]
30	**27**	**10**	5	2.5	92

[a] Unless otherwise stated, reaction conditions were as follows: room temperature, ketone (5−20 mol % as indicated), 2 mmol of substrate, 3 mmol of Oxone, 9.3 mmol of $NaHCO_3$, 9 mL of CH_3CN, 6 mL of aqueous Na_2·EDTA solution (4×10^{-4} M). [b] Ketone **7** was precipitated with hexane as a white solid (∼80% recovery). Ketone **10** was purified by flash column chromatography (∼80% recovery). [c] Time for epoxidation to complete as shown by TLC or GC analysis. [d] Isolated yield.

(22) As revealed by the X-ray structure of ketone **7**, both methyl groups and phenyl rings are in equatorial positions. Crystal data: ketone **7**, $C_{21}H_{26}NO^+CF_3SO_3^-$, monoclinic, $P2_1/n$ (No. 14) with a = 11.214(2) Å, b = 18.374(3) Å, c = 11.511(2) Å, β = 105.82(2)°, V = 2282.0(7) Å^3, Z = 4, D_c = 1.332 g cm^{-1}, with 1822 reflections refined on 3248 reflections having $I > 3.0\sigma(I)$, R = 0.066 and R_w = 0.092 (the details of the X-ray analysis are provided as Supporting Information).

(23) Burkey, T. J.; Fahey, R. C. *J. Org. Chem.* **1985**, *50*, 1304.

shorter period of time (1.5−5 h). More importantly, we found that the in situ epoxidation of olefins can be performed directly with 5 mol % of tetrahydrothiopyran-4-one, which is oxidized immediately by Oxone to ketone **10** during the epoxidation reactions. For example, with 5 mol % of tetrahydrothiopyran-4-one, substrates **15**, **17** (20 mmol each), and **24** (100 mmol) were epoxidized in excellent isolated yields of epoxides (91−96%).[25] We believe that the method for in situ epoxidation of olefins catalyzed by ketone **10** with inexpensive Oxone as terminal oxidant should make the dioxirane a benchtop reagent for other organic oxidation reactions.

Conclusion

We have demonstrated that efficient ketone catalysts can be developed by using the field effect. Future efforts will be devoted to explore other important factors for the catalytic efficiency of ketones in epoxidation reactions.

Experimental Section

General Methods. The ketones **1**, **2**, **8** and **9**, tetrahydrothiopyran-4-one, olefins, and Oxone were purchased from Aldrich Chemical Co. and used without further purification. Ketone **3** was prepared according to the literature procedure.[7]

Preparation of Ketone 4. To a CH_3CN solution (5 mL) of *N*-methylpiperidone (**1**) (2 g, 17.7 mmol) was added benzyl bromide (2.1 mL, 17.7 mmol) dropwise at room temperature under N_2 atmosphere. Precipitation occurred gradually. After being stirred for 5 min, the reaction mixture was evaporated in vacuo to afford **4a** as a pale yellow solid, which was used in the next step without further purification. To a solution of **4a** (2 g, 7.04 mmol) in CH_3CN (10 mL) and H_2O (10 mL) was added silver trifluoromethanesulfonate (1.8 g, 7.04 mmol) portionwise over 2 min at room temperature. The precipitation of yellow silver bromide was observed immediately. After being stirred for 2 h, the reaction mixture was filtered through a plug of Celite, and the filtrate was concentrated at low temperature under reduced pressure until the product began to crystallize. The precipitate was collected by filtration and washed with a small portion of cold water (8 mL). The resulting solid was dried in vacuo overnight to give **4** (1 g, 40% yield) as a white solid: mp 167−168 °C; ^{1}H NMR (300 MHz, CD_3CN) δ 7.62−7.51 (m, 5H), 4.63 (s, 2H), 3.80−3.60 (m, 4H), 3.13 (s, 3H), 2.92−2.64 (m, 4H); ^{13}C NMR (125.76 MHz, CD_3CN) δ 200.95, 134.11, 131.87, 130.20, 127.77, 122.1 (q, J = 321.6 Hz), 69.28, 59.43, 47.11, 35.78; IR (KBr) 3400 (br, hydrate) cm^{-1}; HRMS (FAB +ve) for $C_{13}H_{18}NO$ (M^+) calcd 204.1380, found 204.1383; MS (FAB +ve) *m*/*z* 222 ($M^+ + H_2O$, 100), 204 (M^+, 19), 154 (13), 91 (23); MS (FAB −ve) *m*/*z*, 149 ($^-$OTf, 100).

General Procedure for Preparation of Ketones 5−7. Preparation of Ketone 5. To a solution of **5c** (2.5 g, 9.4 mmol) in CH_2Cl_2 (45 mL) at 0 °C under N_2 atmosphere was added methyl trifluoromethanesulfonate (1.5 mL, 13.3 mmol). After 10 min, the reaction mixture was warmed to room temperature and stirred for another 6 h. The mixture was concentrated in vacuo to give a solid, which was recrystallized from EtOAc/hexane (v/v = 1:4, 10 mL) to afford **5** (3.8 g, 94% yield) as a white solid: mp 205.0−205.5 °C; ^{1}H NMR (300 MHz, CD_3CN) δ 7.61−7.53 (m, 10H), 5.18 (d, J = 13.9 Hz, 2H), 3.67 (t, J = 17.1 Hz, 2H), 3.00 (s, 3H), 2.82 (d, J = 17.1 Hz, 2H), 2.61 (s, 3H); ^{13}C NMR (67.94 MHz, CD_3CN) δ 199.31, 131.30, 130.09, 129.34, 121.04 (q, J = 320.7 Hz), 74.96, 50.59, 41.32, 37.13; IR (KBr) 1739 cm^{-1}; MS (FAB +ve) *m*/*z* 280 (M^+, 68), 134 (100); MS (FAB −ve) *m*/*z* 149 ($^-$OTf, 100). Anal. Calcd for $C_{20}H_{22}F_3O_4NS$: C, 55.94; H, 5.16; N, 3.26. Found: C, 56.08; H, 5.12; N, 3.43.

Ketone 6 (82% yield as a white solid): mp 199−200 °C; ^{1}H NMR (300 MHz, CD_3CN) δ 7.63−7.53 (m, 10H), 5.17 (dd, J = 14.4 Hz, 3.2 Hz, 1H), 4.88 (d, J = 12.8 Hz, 1H), 3.74 (dd, J = 17.0 Hz, 14.4 Hz, 1H), 3.64−3.53 (m, 1H), 3.04 (s, 3H), 2.84 (dd, J = 17.0 Hz, 3.2 Hz, 1H), 2.58 (s, 3H), 0.85 (d, J = 6.6 Hz, 3H); ^{13}C NMR (67.94 MHz, CD_3CN) δ 202.20, 135.36, 132.39, 132.20, 131.25, 130.69, 130.41, 129.59, 122.15 (q, J = 320.7 Hz), 81.72, 75.93, 52.41, 44.69, 42.11, 38.83, 12.33; IR (KBr) 1737 cm^{-1}; MS (FAB +ve) *m*/*z* 294 (M^+, 100), 154 (22), 134 (28); MS (FAB -ve) *m*/*z* 149 ($^-$OTf, 100). Anal. Calcd for $C_{21}H_{24}F_3O_4NS$: C, 56.88; H, 5.45; N, 3.16. Found: C, 57.04; H, 5.43; N, 3.29.

Ketone 7 (93% yield as a white solid): mp 270.0−270.5 °C; ^{1}H NMR (300 MHz, CD_3CN) δ 7.67−7.48 (m, 10H), 4.87 (d, J = 13.0 Hz, 2H), 3.72−3.61 (m, 2H), 3.11 (s, 3H), 2.54 (s, 3H), 0.85 (d, J = 6.5 Hz, 6H); ^{13}C NMR (67.94 MHz, CD_3CN) δ 204.19, 135.40, 132.19, 130.70, 130.61, 130.43, 129.94, 122.14 (q, J = 320.7 Hz), 81.66, 53.11, 44.10, 39.48, 12.65; IR (KBr) 1727 cm^{-1}; MS (FAB +ve) *m*/*z* 308 (M^+, 100), 134 (26); MS (FAB −ve) *m*/*z* 149 ($^-$OTf, 100). Anal. Calcd for $C_{22}H_{26}F_3O_4NS$: C, 57.76; H, 5.73; N, 3.06. Found: C, 57.85; H, 5.71; N, 3.18.

Preparation of Ketone 10. To a CH_3CN solution (4.5 mL) of tetrahydrothiopyran-4-one (0.4 g, 3.4 mmol) at room temperature was added an aqueous Na_2·EDTA solution (3 mL, 4 × 10^{-4} M). To this mixture was added in portions a mixture of Oxone (6.3 g, 10.3 mmol) and sodium bicarbonate (2.7 g, 32.0 mmol) within 30 min. The reaction was complete after 40 min. The reaction mixture was diluted with CH_2Cl_2 (80 mL), dried over anhydrous $MgSO_4$, and filtered. The filtrate was concentrated to dryness under reduced pressure to afford ketone **10** as a white solid (0.38 g, 75% yield): mp 168−170 °C (lit.[17] 163−170 °C); ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.39 (t, J = 6.8 Hz, 4H), 2.99 (t, J = 6.8 Hz, 4H); ^{13}C NMR (67.94 MHz, $CDCl_3$) δ 202.09, 49.60, 38.22; IR (CH_2Cl_2) 1725 cm^{-1}.

General in Situ Epoxidation Procedure. To a CH_3CN solution (9 mL) of olefin (2 mmol) and ketone **7** (10−20 mol % as stated in Table 2) or **10** (5−10 mol % as stated in Table 2) at room temperature was added an aqueous Na_2·EDTA solution (6 mL, 4 × 10^{-4} M). To this mixture was added in portions a mixture of Oxone (1.84 g, 3 mmol) and sodium bicarbonate (0.78 g, 9.3 mmol) over the reaction period. The reaction progress was followed by TLC or GC analysis, and the reaction was worked up according to the following procedures.

Workup Procedure A (For Ketone 7, Substrates 13, 15, 17−19, 21−24, and 26). The reaction mixture was diluted with CH_2Cl_2 (50 mL). The organic phase was separated, dried over anhydrous $MgSO_4$, filtered, and concentrated. The residue was extracted with hexane/CH_2Cl_2 (v/v = 99.5:0.5, 2 × 50 mL) and then filtered to give ketone **7** as a white solid (~80% recovery). The filtrate was concentrated under reduced pressure, and the residue was purified by flash column chromatography to give epoxide.

Workup Procedure B (For Ketone 7, Substrates 14, 16, 20, 25, and 27). The reaction mixture was extracted with

(24) Epoxidation of substrates **14**, **15**, and **27** on a 1−2 mmol scale catalyzed by either 4-oxopiperidinium salts (10 mol %) in a biphasic CH_2Cl_2−H_2O system (pH 7.8) or α,α′-bis(ammonium) ketone (10 mol %) in a homogeneous CH_3CN−H_2O system (pH 6.0) at 0 °C was complete in 8−24 h with 10 equiv of Oxone (see refs 7 and 13).

(25) Epoxidation reactions of substrates **15** and **17** were complete in 1.7 and 3.5 h with 96% and 91% isolated yields of epoxides, respectively. Reaction conditions were as follows: room temperature, 1 mmol of tetrahydrothiopyran-4-one, 20 mmol of substrate, 30 mmol of Oxone, 93 mmol of $NaHCO_3$, 90 mL of CH_3CN, 60 mL of aqueous Na_2·EDTA solution (4 × 10^{-4} M). Epoxidation of substrate **24** was complete in 2 h with 92% isolated yield of the epoxide. Reaction conditions were as follows: room temperature, 5 mmol of tetrahydrothiopyran-4-one, 100 mmol of substrate **24**, 150 mmol of Oxone, 465 mmol of $NaHCO_3$, 450 mL of CH_3CN, 300 mL of aqueous Na_2·EDTA solution (4 × 10^{-4} M).

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n-pentane (2 × 50 mL). The combined pentane layers were dried over anhydrous $MgSO_4$, filtered through a plug of silica gel, and concentrated under reduced pressure at low temperature to afford epoxide. The mixed CH_3CN/H_2O layers were then extracted with CH_2Cl_2 (2 × 50 mL). The combined organic layers were dried over anhydrous $MgSO_4$, filtered, and concentrated to give ketone **7** as a white solid (~80% recovery).

Workup Procedure C (For Ketone 10, Substrates 13, 15, 17−19, 21−24, and 26). The reaction mixture was extracted with EtOAc (2 × 50 mL). The combined organic layers were dried over anhydrous $MgSO_4$, filtered, and concentrated. The residue was purified by flash column chromatography to afford epoxide and ketone **10** (~80% recovery).

Workup Procedure D (For Ketone 10, Substrates 14, 16, 20, 25, and 27). The reaction mixture was extracted with *n*-pentane (2 × 50 mL). The combined pentane layers were dried over anhydrous $MgSO_4$, filtered through a plug of silica gel, and concentrated under reduced pressure at low temperature to afford epoxide. The mixed CH_3CN/H_2O layers were then extracted with EtOAc (2 × 50 mL). The combined organic layers were dried over anhydrous $MgSO_4$, filtered, and concentrated. The residue was purified by flash column chromatography to afford ketone **10** (~80% recovery).

General Procedure for Determination of the Hydration Equilibrium Constants for Ketones 1, 3−7, 9, and 10. A solution of ketone (0.1 mmol) in CD_3CN (1.5 mL) and D_2O (1 mL) was prepared. A portion of this solution (0.5 mL) was transferred to an NMR tube. After the sample was equilibrated for 10 min, the ^1H and ^{13}C NMR spectra were taken at 20 °C. In addition, two more measurements were taken after the sample was equilibrated for 1 and 24 h. For the detail assignments of the chemical shift values of the ketone and its hydrate see the Supporting Information.

Acknowledgment. This work was supported by The University of Hong Kong and Hong Kong Research Grants Council. Y.-C.Y. and M.-K.W. are the recipients of the University Postdoctoral Fellowships. We thank Dr. K. K. Cheung for determination of the X-ray structure of ketone **7** and Prof. D. T. W. Chan for determination of the HRMS of ketone **4**.

Supporting Information Available: Characterization data for the product epoxides shown in Table 2; determination of hydration equilibrium constants for ketones **1**, **3**−**7**, **9**, and **10**; ^1H and ^{13}C NMR spectra for ketone **4**; X-ray structural analysis of ketone **7** containing tables of atomic coordinates, thermal parameters, bond lengths, and angles (20 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

JO981270R