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LETTERS

An efficient and robust fluoroketone catalyst epoxidation

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Abstract—The fluoroalkylketone **2** is an efficient catalyst in the epoxidation reaction using Oxone® as oxidant. In hexafluoro-2-propanol (HFIP), the ketone can be used in a catalytic amount (1 or 5 mol%) with only 1.5 equiv. of Oxone®. The reaction gave good yields of epoxides for a number of olefin substrates, included low reactive ones. © 2001 Elsevier Science Ltd. All rights reserved.

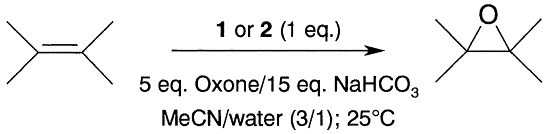
Dioxiranes have been shown to be remarkably promising oxidation reagents for the epoxidation of olefins.[1] Dimethyldioxirane[2] and methyl(trifluoromethyl)-dioxirane[3] are the most widely used. They are generated from the parent ketone with Oxone® and can be used in situ,[4] or isolated.[3] Methyl(trifluoromethyl)dioxirane exhibits the highest reactivity among dioxiranes reported so far. However, the starting trifluoroacetone is expensive, volatile (22°C) and until recently it was used in excess. Consequently, efforts have been focused to improve the use of trifluoroacetone and other fluoroalkylketones as catalysts in epoxidation reactions in the presence of hydrogen peroxide or Oxone®.[1g–i,5,6] We present here our results on a new fluoroalkylketone, which is particularly stable and efficient in the dioxirane-mediated epoxidation reaction.

At first we envisaged using a non volatile ketone bearing a long perfluorochain instead of the CF_3 group. We chose the ketone **1** ($C_7F_{15}COCH_3$: bp 120°C) already described in the literature.[7]

The potency of the ketone **1** was evaluated in the epoxidation reaction of cyclooctene and dodecene. The reaction was conducted using one equivalent of ketone **1** in homogeneous conditions (MeCN/water)[8] in the presence of $NaHCO_3$ and 5 equivalents of Oxone® was added by syringe pump over 2 h (Table 1).

Under these conditions, and despite the low solubility of ketone **1** in MeCN/water, conversion to epoxide was complete. Epoxides were isolated in high yield (≈90%).

Table 1. Epoxidation reaction in MeCN–water with ketones **1** or **2**



Olefin	Ketone	Time (h)[a]	Epoxide/olefin	Recovered ketone[b]	Yield (%)[c]
Cyclooctene	**1**	2	100/0	Traces	96
Dodecene	**1**	4	100/0	Traces	89
Cyclooctene	**2**	1	100/0	>98	96
Dodecene	**2**	2	100/0	>98	90

[a] After slow addition of Oxone®.
[b] Determined by GC and ^{1}H NMR of the crude mixture.
[c] Isolated yield.

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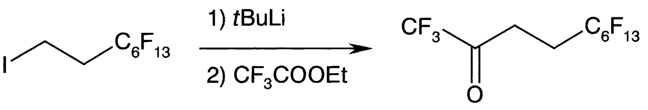
However, according to GC and ^1H NMR analysis, after completion of the reaction the ketone **1** was present only in trace amounts. Although the Baeyer–Villiger oxidation is the likely decomposition pathway, no ester could be detected in the crude product. The aqueous phase was then acidified and work-up afforded the acid $C_7F_{15}CO_2H$ (mp: 55–56°C). This clearly shows that as soon as the ketone catalyst bears a methyl substituent, the Baeyer–Villiger process largely affects the ketone stability. This is consistent with earlier observations concerning trifluoroacetone procedures and the fact explains that accurate and specific conditions had to be found to decrease the amount of catalyst.[5,6]

A solution to avoid the catalyst decomposition was to design a more stable ketone. A ketone bearing both a CF_3 group and an alkyl group deactivated by an electron-withdrawing substituent (for example a perfluoro chain) seemed to be a good candidate: the CF_3 group should maintain the high oxidative potency, and the electron-withdrawing substituent of the alkyl moiety should deactivate the development of a positive charge on α and β carbons, and hence the migratory aptitude required for the Baeyer–Villiger process.[9] Based on these considerations, the ketone **2** was prepared and tested in an epoxidation reaction.

The ketone **2** was prepared according to Guerrero's conditions,[10] by reacting the corresponding iodide with ethyl trifluoroacetate in the presence of *t*BuLi (89%) (Scheme 1).



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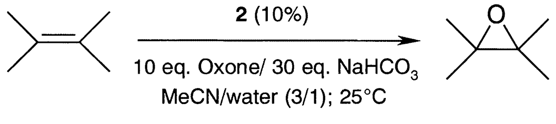
Scheme 1. Preparation of ketone **2**.

Table 2. Catalytic epoxidation reaction in MeCN–water with ketone **2**



Olefin	Time (h)[a]	Oxone® (equiv.)	Epoxide/olefin	Yield (%)[b]
Cyclooctene	3	10	100/0	94
Dodecene	5	10	90/10	79

[a] After 4 h slow addition of Oxone®.

[b] Isolated yield.

Under the same conditions as previously described with ketone **1**, cyclooctene and dodecene reacted quantitatively with one equivalent of ketone **2** in the presence of 5 equivalents of Oxone®, affording the corresponding epoxide. After reaction the ketone **2** was totally present in the crude mixture. No decomposition of the ketone **2** was observed (Table 1).

We could thus explore the reaction using a catalytic amount of ketone **2**. With 10% of ketone **2**, the reaction required a greater quantity of Oxone® (10 equiv.), a longer addition time (4 h) and a longer reaction time. However, all cyclooctene could be converted into epoxide which could be isolated in 94% yield. Interestingly, this ketone **2** was also efficient in affording the epoxide of the poor reactive dodecene in 79% yield (Table 2).

In a search for improving the reactivity, we took into account the great advantages of fluorinated alcohols in oxidation reactions.[11] We thus explored the epoxidation of alkenes using hexafluoro-2-propanol (HFIP) as a solvent instead of acetonitrile.

Reactions of a variety of olefins with ketone **2** in the presence of Oxone® in HFIP are described in Table 3. Only 1.5 equivalents of Oxone® and 6 equivalents of $NaHCO_3$ were required to obtain 100% of conversion, and the reaction was faster. Cyclic, acyclic, *trans*-, *cis*-, disubstituted, trisubstituted and even terminal olefins could be epoxidized in good yields. For those more reactive substrates, the epoxidation was complete using 1 mol% ketone. Only the usually poorly reactive substrates required 5 mol% ketone to gain a high conversion. As expected, in the case of the limonene, the epoxidation occurred selectively on the trisubstituted double bond with 90% conversion (entry 2), and a 1:1 mixture of diastereoisomers was obtained. The use of HFIP as solvent in the dioxirane-mediated epoxidation reaction gave a great improvement in efficiency, probably due to a better solubility of ketone **2** in this solvent.

In summary, we have found an efficient dioxirane-mediated epoxidation reaction using the new fluoroketone **2** as promotor, and using HFIP as solvent. This process presents the following advantages: fluoroketone **2** is easily prepared and handled, it does not suffer from Baeyer–Villiger oxidation and then it can be used in 1–5 mol% amount with only 1.5 equiv. of Oxone®.

Acknowledgements

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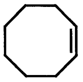
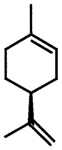
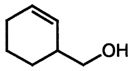
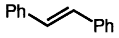
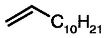
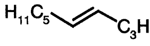
Table 3. Catalytic epoxidation reaction in HFIP/water with the ketone **2**[a]

Entry	Olefin	Mol% ketone **2**	Time add. (h)	Time (h)[b]	Yield (%)[c]
1		1	2	0.3	81[12]
2		1	4	0.5	71[d,13]
3		1	4	0.5	68[e,14]
4		5	4	0.5	93[15]
5		5	4	0.5	92[12]
6		5	4	0.5	96[16]

[a] Reactions were performed as follows: substrate (1.8 mmol), ketone **2** (1 or 5% mmol) and $NaHCO_3$ (10.8 mmol) were placed in a 3/1 mL (entries 1–3, 6) or 12/4 mL (entries 4, 5) mixture of HFIP:water (EDTA 10^{-4} mol/L) under vigorous stirring. A solution of Oxone® (2.7 mmol) dissolved in 10 mL of water was added via a syringe pump over the time indicated above.

[b] After addition of Oxone®.

[c] Yield of isolated product.

[d] 10% of starting material recovered, 1:1 mixture of diastereoisomers.

[e] 1.5:1 mixture of diastereoisomers (not determined).

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CF_3CO_2Et (4.5 g, 31.6 mmol) was added. The solution was stirred for 30 min and was then allowed to warm to 0°C. After 1 h, the solution was quenched with saturated ammonium chloride solution, the layers were separated and the aqueous phase was extracted with Et_2O (3×50 mL). The combined organic phases were dried ($MgSO_4$) and evaporated to afford after chromatography on silica gel (pentane/Et_2O, 80:20), pure fluoroketone **2** as a colorless liquid (8.32 g, 89%): bp 95–96°C; IR (neat) 1772 cm^{-1}; ^{19}F NMR ($CDCl_3$) δ −126.3 (m, 2F), −123.6 (m, 2F), −123.0 (m, 2F), −122.0 (m, 2F), −114.5 (m, 2F), −81.0 (t, $J_{F-F}=10$ Hz, 3F, $CF_3(CF_2)_5$), −79.3 (s, 3F, CF_3); ^{1}H NMR ($CDCl_3$) δ 3.1 (t, $J=7.5$ Hz, 2H), 2.6 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 188.7 (q, $^{2}J_{C-F}=37$ Hz, $CF_3\mathit{C}O$), 115.0 (q, $^{1}J_{C-F}=291$ Hz, $\mathit{C}F_3CO$), 124.0–98.0 (m, C_6F_{13}), 27.9 (t, $^{3}J_{C-F}=3.5$ Hz, $\mathit{C}H_2CH_2C_6F_{13}$), 24.4 (t, $^{2}J_{C-F}=24$ Hz, $\mathit{C}H_2C_6F_{13}$).

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