Pergamon

TETRAHEDRON

Tetrahedron 58 (2002) 3993–3998

Design of fluoroketones as efficient reagents for epoxidation reactions in hexafluoropropan-2-ol

Julien Legros, Benoit Crousse,* Danièle Bonnet-Delpon* and Jean-Pierre Bégué

Laboratoire BioCIS associé au CNRS, Centre d'Etudes Pharmaceutiques, rue J.B. Clément, F-92296 Chatenay-Malabry, France

This paper is dedicated to Professor Takeshi Nakai on the occasion of his 60th birthday

Received 25 October 2001; revised 20 December 2001; accepted 16 January 2002

Abstract—Comparative studies on mediated epoxidation reaction using Oxone® as primary oxidant and various fluoroketones as reagents, revealed that ketone **3** is very efficient, in particular when used in hexafluoroisopropanol (HFIP) as solvent. It does not suffer from Baeyer–Villiger reaction and can be used in a catalytic amount (1–5 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. © 2002 Published by Elsevier Science Ltd.

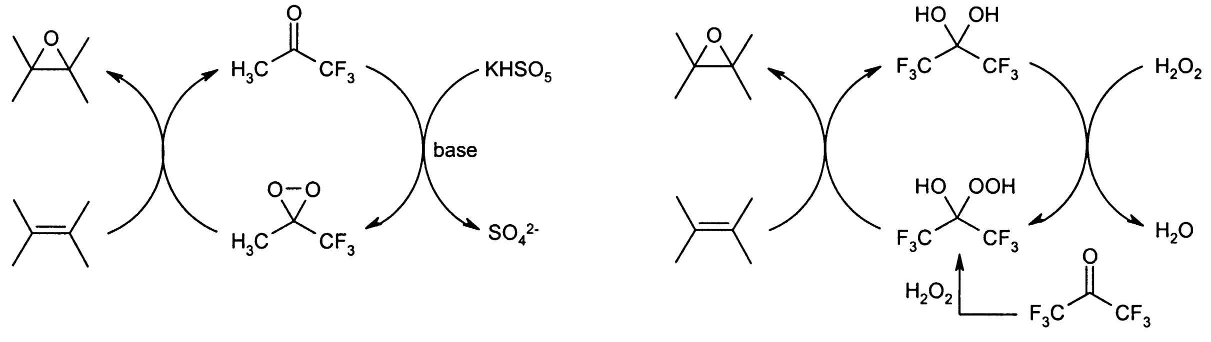
1. Introduction

Fluoro analogs of acetone have been shown to be precursors of very efficient epoxidation reagents. For instance, trifluoroacetone is precursor of the methyl(trifluoromethyl)-dioxirane which is the most powerful dioxirane known.[1] This latter is generated from ketone with Oxone®[2] and can be used in situ,[3] or isolated.[4] Hexafluoroacetone acts differently: in presence of concentrated hydrogen peroxide, it provides 2-hydroperoxyhexafluoropropan-2-ol (HPHI) which is the oxidizing intermediate in epoxidation reaction.[5] In both cases, the epoxidation reaction occurs through a catalytic cycle (Scheme 1).

Despite of their high oxidizing power, these reagents and methods present some drawback. Both starting ketones are expensive and/or volatile (bp CF_3COCH_3: 22°C). Trifluoroacetone undergoes a Baeyer–Villiger oxidation and has to be used in large excess.[4d] Hexafluoroacetone was used until recently only under hard conditions (90% H_2O_2 at reflux of the solvent).[5c,d] Consequently, great efforts have been focused to improve the use of fluoroketones as catalysts in epoxidation reaction with Oxone®[6] or H_2O_2,[7] and great improvements have been achieved. We report here our comprehensive investigations on the design of new fluorinated ketones in order to obtain the following improvements: easy handling, stability towards competitive oxidation process (Baeyer–Villiger reaction), efficiency in Oxone®-mediated epoxidation, recovering and/or use in catalytic conditions.

2. Results and discussion

Our first approach to improve trifluoroacetone and hexafluoroacetone catalysis in epoxidation reaction, was to



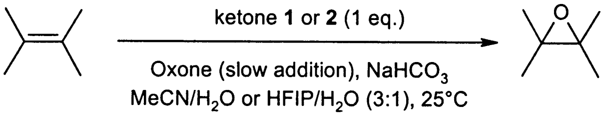
Scheme 1. Cycles of epoxidation reaction with oxidizing reagents derived from tri- and hexafluoroacetone.

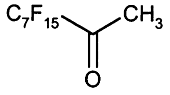
Keywords: epoxidation; fluoroketones; Oxone®; hydrogen peroxide; HFIP; fluorous chain.

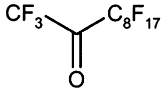
* Corresponding authors. Tel.: +33-1-46-83-57-39; fax: +33-1-46-83-57-40; e-mail: benoit.crousse@cep.u-psud.fr; daniele.bonnet-delpon@cep.u-psud.fr

PII: S0040-4020(02)00252-1

Table 1. Epoxidation reaction with Oxone® and ketone **1** or **2** in MeCN and in HFIP




1


2

Entry	Olefin	Ketone	Oxone® (equiv.)[a]	Add. time (h)	Solvents	Time (h)[b]	Olefin/epoxide[c]	Yield (%)[d]
1	Cyclooctene	**1**	5	2	MeCN/H_2O	3	0:100	96
2	Dodecene	**1**	5	2	MeCN/H_2O	4	0:100	89
3	Cyclooctene	**1**	2.5	1	HFIP/H_2O	1	0:100	78
4	Dodecene	**1**	2.5	1	HFIP/H_2O	2	0:100	95
5	Dodecene	**2**	2.5	2	HFIP/H_2O	1	30:70	–
6	Dodecene	**2**	4	2	HFIP/H_2O	0	0:100	90

Olefin (0.9 mmol), fluoroketone **1** or **2** (0.9 mmol), $NaHCO_3$ (18 mmol, entry 1, 2; or 9 mmol, entry 3–5; or 14.4 mmol, entry 6) in a 3:1 mixture of HFIP (or MeCN)/aqueous EDTA (10^{-4} mol L^{-1}) (4 mL), and Oxone® (4.5 mmol, 2.25 or 3.6 mmol) in aqueous EDTA (10^{-4} mol L^{-1}) (10 mL).

[a] Per mol of olefin.

[b] After slow addition of Oxone®.

[c] Determined by GC.

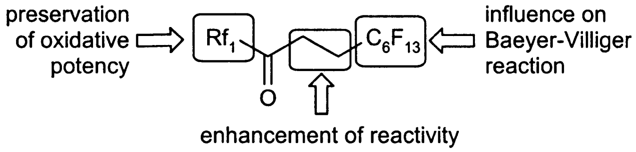
[d] Yield of isolated product.

replace one trifluoromethyl group by a larger perfluoroalkyl group (Rf). Thus we envisaged to design and synthesize highly fluorinated analogs of trifluoroacetone and hexafluoroacetone. Ketone **1** ($C_7F_{15}COCH_3$, bp: 120°C)[8] and ketone **2** ($CF_3COC_8F_{17}$),[9] already described in literature, were chosen as analogs of trifluoroacetone and hexafluoroacetone respectively. Potency of ketone **1** was evaluated in the epoxidation reaction of cyclooctene and of the poor reactive dodecene under the usual conditions of oxidation with Oxone®. The reaction was conducted using 1 equiv. of ketone **1** in MeCN/water at 25°C, in the presence of $NaHCO_3$ (20 equiv.); Oxone® (5 equiv.), dissolved in water, was added by a syringe pump over 2 h. Despite a low solubility of **1** in MeCN/water, conversion in epoxides was complete and products were isolated in high yields (Table 1, entries 1, 2). Conditions of reaction could be improved by using hexafluoroisopropanol (HFIP) as solvent instead of acetonitrile. Indeed fluorinated alcohols have been shown to be very efficient and selective solvents in various oxidation reactions (oxidation of sulfides[10] and of thiols,[11] epoxidation,[6a,7b,c,12] and Baeyer–Villiger reaction[13]). Moreover, in these solvents, both fluorinated compounds and water are miscible.

Under these new conditions, reaction was faster and only 2.5 equiv. of Oxone® and 10 equiv. of $NaHCO_3$ were required for a complete conversion of cyclooctene and dodecene into corresponding epoxides (Table 1, entries 3, 4). This is another example of the improvement of the oxidation processes in fluorinated alcohols. Besides an enhanced solubility of the ketone in HFIP, an activation of the O–O bond cleavage by strong hydrogen bonding with HFIP, can also be evoked. Such an explanation has previously been advanced for activation of hydrogen peroxide.[10a,b]

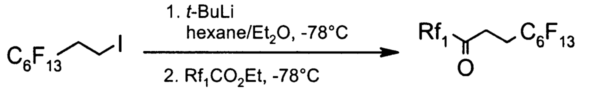
These first experiments demonstrated that ketone **1** is very efficient in the Oxone® oxidation system and easier to handle than trifluoroacetone. However, after completion of the reaction ketone **1** was present only in traces, and the acid $C_7F_{15}CO_2H$ was recovered in the aqueous phase after acidification. This clearly shows that ketone **1** undergoes a Baeyer–Villiger oxidation in Oxone® system. Conversely, the perfluoroketone **2** is unlikely to undergo the Baeyer–Villiger reaction due to the electronwithdrawing character of fluorine atoms.[14,15] However there are no precedent of use of perfluoroketones in epoxidation reaction with Oxone®.[16] Ketone **2** was prepared according to Chen's procedure[9] and was obtained as the corresponding hydrate. Its efficiency was investigated in the epoxidation of dodecene with Oxone®, under the improved conditions (HFIP) described for ketone **1** (Table 1, entries 5, 6). With 2.5 equiv. of Oxone®, a 70% conversion was obtained; 4 equiv. of Oxone® were required for a complete conversion into oxirane. This clearly shows that the system perfluoroketone/Oxone® can be used in epoxidation reaction, when performed in HFIP, but is less efficient than the semi-perfluoroketone/Oxone®. At this stage of this study, it can be concluded that (i) oxidizing efficiency is retained by the replacement of the CF_3 group of the trifluoroacetone by a longer Rf chain, although different reaction conditions do not allow an accurate comparison; however the competitive Baeyer–Villiger process could not be avoided, (ii) presence of Rf chains on both sides of ketone seems to deactivate the ketone as catalyst.

We thus turned to a compromise to design more efficient ketones. A ketone bearing an Rf_1 group on one side, and, on the other side, a perfluorochain Rf_2 (C_6F_{13}) separated from the carbonyl by a two-methylene spacer, was considered as a good candidate. The first Rf_1 group should maintain the high oxidative potency; the presence of the two-methylene spacer should minimize the deactivation due to the second Rf_2 chain; the electronwithdrawing effect of the Rf_2



Scheme 2. Design of ketones **3–5** and expected effects of the structure.

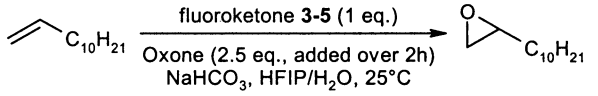
Table 2. Synthesis of fluoroketones **3–5**



Entry	Rf_1	Fluoroketone	Yield (%)[a]
1	CF_3	**3**	89
2	C_3F_7	**4**	69
3	C_7F_{15}	**5**	68

[a] Yield of isolated product.

Table 3. Epoxidation reaction of dodecene in HFIP/H_2O with fluoroketones **3–5**



Ketone	Time (h)[a]	Olefin/ epoxide[b]	Recovered ketone[c] (%)	Yield (%)[d]
3	1	0:100	>98	95
4	1	45:55	>98	n.c.
5	1	100:0	>98	0

Dodecene (1.8 mmol), fluoroketone (1.8 mmol), $NaHCO_3$ (18 mmol) in a 3:1 mixture of HFIP/aqueous EDTA (10^{-4} mol L^{-1}) (16 mL), and Oxone® (4.5 mmol) in aqueous EDTA (10^{-4} mol L^{-1}) (10 mL).

[a] After addition of Oxone®.

[b] Measured by GC. No byproduct observed.

[c] Measured by GC in the crude mixture.

[d] Yield of isolated product.

substituent was anticipated to disfavor the Baeyer–Villiger process[14,15] (Scheme 2). Three ketones (**3–5**) were thus prepared (Rf_1=CF_3, C_3F_7 and C_7F_{15}).

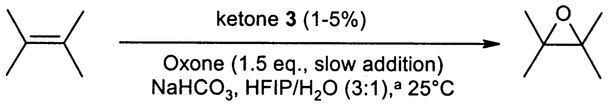
Ketones **3–5** were readily obtained following Guerrero's procedure,[17] from the commercial iodide **6** and the ethyl perfluoroalkylcarboxylates (Table 2). The potency of ketones **3–5**, used stoichiometrically, was evaluated in the epoxidation reaction of dodecene with Oxone®, $NaHCO_3$, in HFIP/water at 25°C (Table 3).

With 2.5 equiv. of Oxone®, after 1 h of reaction, conversion rate of dodecene to the corresponding epoxide was 100, 55 and 0% with ketones **3**, **4** and **5**, respectively, and these ketones were found unchanged (>98% by GC analysis) when the reaction was stopped. Oxidative potency of fluoroketones in the Oxone® system clearly decreases with the Rf_1 chain length. Such an influence of the Rf length has already been noticed in the oxidizing fluoroketone/H_2O_2 system.[7b]

Further investigations were then conducted with the most efficient ketone **3**. Considering its stability in the reaction medium, ketone **3** could a priori be used in stoichiometric amount and recovered, or be used in a catalytic amount. All our attempts to recover the ketone **3** by technics of fluorous phase separation, by use of liquid–liquid extraction[18] or by separation over fluorous reverse phase silica gel,[19] were not very fruitful: less than 50% of ketone could be recovered. Oxidation reactions were then investigated using ketone **3** catalytically. Reactions were performed in HFIP with various olefins (Table 4).

Cyclic, acyclic, *trans*-, *cis*-, disubstituted, trisubstituted and even terminal olefins were all converted into epoxides in good yields. First, with the use of HFIP as solvent,[20] required amounts of Oxone® could be decreased to 1.5 equiv., instead of 5 equiv. And with the more reactive substrates (entries 1–3), the epoxidation was complete by using only 1 mol% of ketone **3**. With the poor reactive olefins (entries 4–6) 5 mol% catalyst were required for a complete reaction. As expected, in the case of limonene, the epoxidation occurred selectively on the trisubstituted double bond (entry 2), and a 1:1 mixture of stereoisomers was obtained. In all cases, epoxides were isolated in high yields.

Table 4. Catalytic epoxidation reaction with Oxone® and ketone **3** in HFIP/H_2O



Entry	Olefin	Ketone **3** (mol%)	Add. time (h)	Time (h)[a]	Epoxide	Yield (%)[b]
1	Cyclooctene	1	2	0.3	**6**	81
2	(S)-Limonene	1	4	0.5	**7a**, **b**[c]	71
3	Cyclohex-3-ene-1-methanol	1	4	0.5	**8a**, **b**[d]	68
4	*trans*-Stilbene	5	4	0.5	**9**	93
5	Dodec-1-ene	5	4	0.5	**10**	92
6	*trans*-Dec-4-ene	5	4	0.5	**11**	96

1.8 mmol of olefin in 4 mL (entry 1–3) or in 16 mL of HFIP/aqueous EDTA (10^{-4} mol L^{-1}).

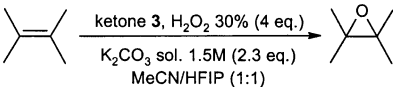
[a] After addition of Oxone®.

[b] Except where indicated, reaction afforded 100% conversion. Yield of isolated product.

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

[d] 1.5:1 mixture of diastereoisomers, observed by GC, (not determined).

Table 5. Epoxidation reaction with ketone **3** in H_2O_2/MeCN oxidant system



Olefin	Ketone **3** (mol%)	Solvent	Time (h)	Olefin/epoxide[a]
Cyclooctene	10	MeCN	6.5	50:50
Cyclooctene	1	MeCN/HFIP	16	0:100
Dodecene	10	MeCN/HFIP	24	80:20

Reactions were carried out with olefin (1.8 mmol), ketone **3** (0.02–0.18 mmol), H_2O_2 aq. 30% (7.2 mmol) and aqueous K_2CO_3 solution (1.5 mol. L^{-1} in 10^{-4} mol. L^{-1} EDTA) in MeCN (2 mL, entry 1), or MeCN/HFIP (2 mL, entry 2–3) at 0°C for 1 h, then rt.

[a] Measured by GC.

For comparison, ketone **3** was also evaluated as promotor in another oxidation system. Recently, a very efficient system for epoxidation of olefins has been described with trifluoroacetone (10–30 mol%), with H_2O_2 30% (4 equiv.), in MeCN as solvent, at pH 11.[7a] The first step of the process is supposed to be the formation of peroxyimidic acid resulting from the reaction between MeCN and H_2O_2, which further generates the dioxirane by reacting with trifluoroacetone. This process was carried out with ketone **3** in epoxidation reaction of cyclooctene and dodecene (Table 5). For cyclooctene, with 10% ketone, the conversion rate was only 50% in MeCN even after 24 h. By using HFIP as co-solvent, the conversion could be increased to 100% with only 1% of **3**. Nevertheless, with a poor reactive substrate (dodecene), only 20% conversion of olefin into the corresponding oxide was obtained, even with 10% catalyst. Thus, ketone **3** is much more efficient using Oxone® as primary oxidant.

3. Conclusion

The design of new models of fluoroketones as promotors for epoxidation reactions allowed us to find out the very powerful oxidizing ketone **3** in presence of Oxone®. This ketone is more reactive than perfluoroketone **2**, and more stable than semifluoroketone **1** which suffers from Baeyer–Villiger oxidation. Furthermore, when reaction was performed in hexafluoroisopropanol as solvent, the efficiency of ketones was highly improved. The new fluorinated ketone **3** is easily prepared, efficient in catalytic amount (1–5 mol%) for Oxone® mediated epoxidation of various olefins, even the less reactive ones. This the smallest amount of fluoroketone required for any reported system at the date of today. No restricting conditions (temperature, control of pH) are required and only 1.5 equiv. of Oxone® are sufficient for a high yield of oxiranes.

4. Experimental

^{19}F, ^{1}H and ^{13}C NMR were recorded on a Bruker AC-200 MHz multinuclear spectrometer. Chemical shifts (δ) are given in ppm relative to $CFCl_3$ for ^{19}F NMR, and relative to TMS for ^{1}H and ^{13}C NMR. Except where indicated, $CDCl_3$ was used as a solvent. IR spectra were recorded on a Bruker Vector 22 spectrometer. GC analysis were performed on HP 4890 apparatus equipped with a SE 30 capillary column (l=30 m). HFIP was used as provided, without any purification procedure.

4.1. Preparation of fluoroketones 3–5

4.1.1. Perfluorodecan-2-one 2 (isolated as its hydrate form).[9] Colorless crystals: mp 38°C; IR (neat) ν 3198 cm^{-1}; ^{19}F NMR δ −126.5 (m, 2F), −123.0 (m, 2F), −122.0 (m, 8F), −120.8 (m, 2F), −81.6 (m, 3F, $CF_3(CF_2)_7$), −81.2 (tt, J_{F-F}=10, 1.9 Hz, 3F, CF_3); ^{1}H NMR δ 3.0 (s, OH); ^{13}C NMR ($(CD_3)_2CO$) δ 120.4 (q, $^{1}J_{C-F}$=290 Hz, $CF_3C(OH)_2$), 122–100 (m, C_8F_{17}), 91.9 (m, $C(OH)_2$).

4.1.2. Preparation of 3*H*,3*H*,4*H*,4*H*-perfluorodecan-2-one 3: typical procedure. *t*-BuLi (13.6 mL, 23.2 mmol, 1.7 M in hexane) was added at −78°C under argon to a well-stirred solution of $C_6F_{13}(CH_2)_2I$ (10 g, 21.1 mmol) in a 3:2 mixture of hexane/Et_2O (100 mL). After 5 min, 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 to afford, after chromatography on silica gel (pentane/Et_2O, 80:20), pure ketone **3** as a colorless liquid (8.32 g, 89%): bp 95–96°C; IR (neat) ν 1772 cm^{-1}; ^{19}F NMR 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, $CF_3(Rf_2)$), −79.3 (s, 3F, CF_3); ^{1}H NMR δ 3.1 (t, J=7.5 Hz, 2H), 2.6 (m, 2H); ^{13}C NMR δ 188.7 (q, $^{2}J_{C-F}$=37 Hz, CF_3CO), 115.0 (q, $^{1}J_{C-F}$=291 Hz, CF_3CO), 124.0–98.0 (m, Rf_2), 27.9 (t, $^{3}J_{C-F}$=3.5 Hz, $CH_2CH_2Rf_2$), 24.4 (t, $^{2}J_{C-F}$=24 Hz, CH_2Rf_2).

4.1.3. 5*H*,5*H*,6*H*,6*H*-Perfluorododecan-4-one 4. Starting from $C_3F_7CO_2Et$ (7 g, 28.9 mmol) and $C_6F_{13}(CH_2)_2I$ (5.5 g, 11.6 mmol), afforded pure ketone **4** as a colorless liquid (4.35 g, 69%): IR (neat) ν 1766 cm^{-1}; ^{19}F NMR δ −126.9 (s, 2F, $CF_2(Rf_1)$), −126.4 (m, 2F), −123.8 (m, 2F), −123.2 (m, 2F), −122.2 (m, 2F), −121.4 (q, J_{F-F}=8.7 Hz, 2F, $CF_2CF_3(Rf_1)$), −114.6 (m, 2F), −81.2 (tt, J_{F-F}=9.3, 2.5 Hz, 3F, $CF_3(Rf_2)$), −80.9 (t, J_{F-F}=9.0 Hz, $CF_3(Rf_1)$); ^{1}H NMR δ 3.1 (t, J=7.5 Hz, 2H), 2.5 (m, 2H); ^{13}C NMR δ 191.6 (t, $^{2}J_{C-F}$=27.0 Hz, Rf_1CO), 124–100 (m, Rf_1, Rf_2), 29.7 (t, $^{3}J_{C-F}$=3.5 Hz, $CH_2CH_2Rf_2$), 24.7 (t, $^{2}J_{C-F}$=24 Hz, CH_2Rf_2).

4.1.4. 9*H*,9*H*,10*H*,10*H*-Perfluorohexadecan-8-one 5. Starting from $C_7F_{15}CO_2Et$ (8.3 g, 18.8 mmol) and $C_6F_{13}(CH_2)_2I$ (3.56 g, 7.5 mmol), afforded, after crystallization (Et_2O/petroleum ether), pure ketone **5** as a white solid (3.8 g, 68%): mp 54°C; IR (neat) ν 1758 cm^{-1}; ^{19}F NMR δ −126.5 (m, 4F), −124.0 (m, 2F), −123.2 (m, 4F), −122.4 (m, 6F), −121.8 (m, 2F), −120.5 (m, 2F), −114.8 (m, 2F), −81.2 (m, 6F, 2×CF_3); ^1H NMR δ 3.2 (t, J=7.5 Hz, 2H), 2.5 (m, 2H); ^{13}C NMR ($CDCl_3$, 57°C) δ −191.0 (t, $^2J_{C-F}$=27.0 Hz, Rf_1CO), 124–100 (Rf_1, Rf_2), 29.6 ($CH_2CH_2Rf_2$), 24.7 (t, $^2J_{C-F}$=24 Hz, CH_2Rf_2).

4.2. Catalytic epoxidation of olefin with ketone 3 and Oxone® in HFIP

4.2.1. Epoxidation of *trans*-dec-4-ene: typical procedure. To a solution of *trans*-dec-4-ene (252 mg, 1.8 mmol) in HFIP (2 mL), at 25°C, fluoroketone **3** (40 mg, 0.09 mmol), dissolved in HFIP (1 mL), was added. Then, $NaHCO_3$ (907 mg, 10.8 mmol) and aqueous EDTA (10^{-4} mol L^{-1}) (1 mL) were added, and the mixture was vigorously stirred. A solution of Oxone® (1.66 g, 2.7 mmol) in aqueous EDTA (10^{-4} mol L^{-1}) (10 mL), was added, over 4 h via a syringe pump, to the precedent solution. After the addition, the reaction mixture was maintained under stirring for 0.5 h (reaction was monitored by GC), then poured into 70 mL of water and extracted with Et_2O (3×30 mL). The combined organic phases were washed with brine (40 mL), dried over $MgSO_4$ and solvents were evaporated, to afford, after chromatography on silica gel (petroleum ether/Et_2O, 70:30), pure *trans*-4,5-epoxydecane **11**[21] as a colorless liquid (270 mg, 96%). ^1H NMR δ 2.7–2.6 (m, 2H), 1.6–1.4 (m, 8H), 1.4–1.2 (m, 4H), 1.0–0.8 (m, 6H).

4.2.2. 1,2-Epoxycyclooctane (6).[22] ^1H NMR δ 3.0–2.8 (m, 2H), 2.2–2.0 (m, 2H), 1.7–1.1 (m, 10H).

4.2.3. 1,2-Epoxymenth-8-ene (7a/7b).[23] ^1H NMR δ 4.7 (m, 1H), 4.6 (br, s, 1H), 3.0–2.9 (br t, J=3.0 Hz, 1H/d, J=5.4 Hz), 2.1–1.4 (m, 7H), 1.7–1.65 (s, 3H), 1.32–1.31 (s, 3H).

4.2.4. 3,4-Epoxycyclohexan-1-methanol (8a/8b).[24] ^1H NMR δ 3.5–3.3 (m, 2H), 3.2–3.1 (m, 2H), 2.3–0.9 (m, 8H).

4.2.5. *trans*-Stilbene oxide (9).[25] ^1H NMR δ 7.4 (s, 10H), 3.9 (s, 2H).

4.2.6. 1,2-Epoxydodecane (10).[22] ^1H NMR δ 2.9 (br m, 1H), 2.8 (dd, J=5.1, 4.0 Hz, 1H), 2.5 (dd, J=2.7, 5 Hz, 1H), 1.6–1.2 (m, 18H), 0.9 (t, J=6.0 Hz, 3H).

Acknowledgements

We thank Central Glass Co., Ltd for kindly providing HFIP. We also thank the European Contract of Research Training Network ('Fluorous Phase' HPRN CT 2000-00002) and the European Union (COST-Action 'Fluorous Medium' D12/98/0012).

References

1. For reviews of dioxirane chemistry: (a) Adam, W.; Curci, R.; Edwards, J. O. *Acc. Chem. Res.* **1989**, *22*, 205–211. (b) Murray, R. W. *Chem. Rev.* **1989**, *89*, 1187–1201. (c) Curci, R. *Advances in Oxygenated Processes*; Baumstark, A. L., Ed.; JAI: Greenwich, 1990; Vol. 2, pp. 1–59 Chapter 1. (d) Adam, W.; Hadjiarapoglou, L. P.; Curci, R.; Mello, R. In *Organic Peroxides*, Ando, W., Ed.; Wiley: New York, 1992; pp. 195–219 Chapter 4. (e) Adam, W.; Hadjiarapoglou, L. P. *Topics in Current Chemistry*, Vol. 1645; Springer: Berlin, 1993 pp 45–62. (f) Curci, R.; Dinoi, A.; Rubino, M. F. *Pure Appl. Chem.* **1995**, *67*, 811–822. (g) Denmark, S. E.; Wu, Z. *Synlett* **1999**, 847–859. (h) Denmark, S. E.; Wu, Z.; Grudden, C. M.; Matsuhashi, H. *J. Org. Chem.* **1997**, *62*, 8288–8289. (i) Brown, D. S.; Marples, B. A.; Smith, P.; Walton, L. *Tetrahedron* **1995**, *51*, 3587–3606.
2. Oxone® is the trademark of $2KHSO_5{\cdot}KHSO_4{\cdot}K_2SO_4$.
3. (a) Yang, D.; Wong, M. K.; Yip, Y. C. *J. Org. Chem.* **1995**, *60*, 3887–3889. (b) Edwards, J. O.; Pater, R. H.; Curci, R.; Di Furia, F. *Photochem. Photobiol.* **1979**, *30*, 63–70. (c) Gallopo, A. R.; Edwards, J. O. *J. Org. Chem.* **1981**, *46*, 1684–1688. (d) Cicala, G.; Curci, R.; Fiorentino, M.; Laricchiuta, O. *J. Org. Chem.* **1982**, *47*, 2670–2673.
4. (a) Adam, W.; Asensio, G.; Curci, R.; González-Nuñez, M. E.; Mello, R. *J. Am. Chem. Soc.* **1992**, *114*, 8345–8349. (b) Adam, W.; Curci, R.; González-Nuñez, M. E.; Mello, R. *J. Am. Chem. Soc.* **1991**, *113*, 7654–7658. (c) Mello, R.; Fiorentino, M.; Fusco, C.; Curci, R. *J. Am. Chem. Soc.* **1989**, *111*, 6749–6757. (d) Denmark, S. E.; Forbes, D. C.; Hays, D. S.; DePue, J. S.; Wilde, R. G. *J. Org. Chem.* **1995**, *60*, 1391–1407.
5. (a) Adam, W.; Degen, H. G.; Chantu, R. S. M. *J. Org. Chem.* **1999**, *64*, 1274–1277. (b) Iwahama, T.; Sakaguchi, S.; Ishii, Y. *Heterocycles* **2000**, *52*, 693–705. (c) Biloski, A. J.; Heggs, R. P.; Ganem, B. *Synthesis* **1980**, 810–811. (d) Heggs, R. P.; Ganem, B. *J. Am. Chem. Soc.* **1979**, *101*, 2484–2486. (e) For a review of perhydrate chemistry, see: Ganeshpure, P. A.; Adam, W. *Synthesis* **1996**, 179–188.
6. (a) Legros, J.; Crousse, B.; Bourdon, J.; Bonnet-Delpon, D.; Bégué, J. P. *Tetrahedron Lett.* **2001**, *42*, 4463–4466. (b) Song, C. E.; Lim, J. S.; Kim, S. C.; Lee, K. J.; Chi, D. Y. *Chem. Commun.* **2000**, 2415–2416.
7. (a) Shu, L.; Shi, Y. *J. Org. Chem.* **2000**, *65*, 8807–8810. (b) Van Vliet, M. C. A.; Arends, I. W. C. E.; Sheldon, R. A. *Chem. Commun.* **1999**, 263–264. (c) Van Vliet, M. C. A.; Arends, I. W. C. E.; Sheldon, R. A. *Synlett* **2001**, 1305–1307.
8. Kondo, A.; Iwatsuki, S. *J. Fluorine Chem.* **1984**, *26*, 59–67.
9. Chen, L. S.; Chen, G. J. *J. Fluorine Chem.* **1989**, *42*, 371–387.
10. (a) Ravikumar, K. S.; Bégué, J. P.; Bonnet-Delpon, D. *Tetrahedron Lett.* **1998**, *39*, 3141–3144. (b) Ravikumar, K. S.; Zhang, Y. M.; Bégué, J. P.; Bonnet-Delpon, D. *Eur. J. Org. Chem.* **1998**, 2937–2940. (c) Ravikumar, K. S.; Barbier, F.; Bégué, J. P.; Bonnet-Delpon, D. *J. Fluorine Chem.* **1999**, *95*, 123–125.
11. Kesavan, V.; Bonnet-Delpon, D.; Bégué, J. P. *Synthesis* **2000**, 223–225.
12. (a) For the first examples of HFIP used as co-solvent in catalyzed hydrogen peroxide epoxidation, see: Shryne, T. M. US 4024165 (1977) (Shell), Romanelli, M. G. EP 0096130 (1983) (Exxon). (b) Ravikumar, K. S.; Barbier, F.; Bégué, J. P.; Bonnet-Delpon, D. *Tetrahedron* **1998**, *54*, 7457–7464. (c) Neimann, K.; Neumann, R. *Org. Lett.* **2000**, *2*, 2861–2863.

(d) Van Vliet, M. C. A.; Arends, I. W. C. E.; Sheldon, R. A. *Synlett* **2001**, 248–250.

13. Berkessel, A.; Andreae, M. R. M. *Tetrahedron Lett.* **2001**, *42*, 2293–2295.
14. For reviews of the Baeyer–Villiger oxidation, see: (a) Krow, G. R. *Org. React.* **1993**, *43*, 251–379. (b) Renz, M.; Meunier, B. *Eur. J. Org. Chem.* **1999**, 737–750.
15. Kitazume, T.; Kataoka, J. *J. Fluorine Chem.* **1996**, *80*, 157–158.
16. Epoxidation reaction with hexafluoroacetone/Oxone® has been reported to be unsuccessful: Ref. 4d.
17. Villuendas, I.; Parilla, A.; Guerrero, A. *Tetrahedron* **1994**, *50*, 12673–12684.
18. (a) Horváth, I. T.; Rábai, J. *Science* **1994**, *266*, 72. (b) For a review on extraction with fluorinated solvents, see: Curran, D. P. *Angew. Chem., Int. Ed. Engl.* **1998**, *37*, 1175–1196.
19. For a review on fluorous reverse phase silica gel, see: Curran, D. P. *Synlett* **2001**, 1488–1496.
20. Same reaction performed in trifluoroethanol gave similar results, but in a longer reaction time. In MeOH, no reaction occurred. It has to be noted that when supplied in bulk the price of HFIP can be reasonable.
21. Venturello, C.; D'Aloisio, R. *J. Org. Chem.* **1988**, *53*, 1553–1557.
22. Rocha Gonsalves, A. M. d'A.; Pereira, M. M.; Serra, A. C.; Johnstone, R. A. W.; Nunes, M. L. P. G. *J. Chem. Soc., Perkin Trans. 1* **1994**, 2053–2057.
23. Carman, R. M.; Klika, K. D. *Aust. J. Chem.* **1991**, *44*, 1803–1808.
24. Chini, M.; Crotti, P.; Flippin, L. A.; Macchia, F.; Pineschi, M. *J. Org. Chem.* **1992**, *57*, 1405–1412.
25. Battioni, P.; Renaud, J. P.; Bartoli, J. F.; Reina-Artiles, M.; Fort, M.; Mansuy, D. *J. Am. Chem. Soc.* **1988**, *110*, 8462–8470.