Perfluoroheptadecan-9-one: a selective and reusable catalyst for epoxidations with hydrogen peroxide

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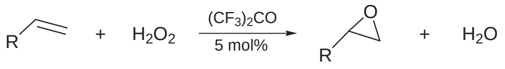
Perfluoroheptadecan-9-one is a selective and mild catalyst for the epoxidation of a wide variety of alkenes with hydrogen peroxide; after the reaction the catalyst can be easily recovered and reused without noticable decomposition.

Following the seminal publication of Horváth and Rábai[1] in 1994 there has been increasing interest in the concept of fluorous biphasic catalysis.[2] The use of catalysts soluble in the fluorous phase facilitates catalyst separation from substrate and products which are soluble in a second (*e.g.* hydrocarbon) phase. Attachment of long perfluoroalkyl groups ('fluorous ponytails') to *e.g.* phosphine ligands, renders metal complexes soluble in fluorocarbons and insoluble in most organic solvents. In most cases catalytic activity is preserved only when the perfluoroalkyl group is not directly attached to the ligand but is separated by a spacer, mostly a –CH_2CH_2– group.[2] In this way the electronic properties of the ligand are not significantly affected by the strongly electron-withdrawing perfluoroalkyl moiety.

A few examples of the application of fluorous biphasic chemistry to catalytic oxidations have been reported.[3] In all the reported cases the unique electron-withdrawing properties of the perfluoroalkyl group were not exploited. On the other hand, the use of hexafluoroacetone as a mild and selective catalyst for the epoxidation of alkenes with highly concentrated hydrogen peroxide (Scheme 1) has been known for more than 25 years.[4]



Scheme 1

Although rates are rather low, the reaction proceeds under very mild conditions and affords very acid-sensitive epoxides in high yields. A major disadvantage, however, is the high volatility of hexafluoroacetone and its application at reflux temperature (80 °C) requires a cryogenic condensor to avoid loss of the catalyst. Our approach to improve this catalyst was to replace the trifluoromethyl groups by larger perfluoroalkyl groups. The advantages are clear: the catalyst is less volatile† and the use of long perfluoroalkyl groups render it highly soluble in a fluorous phase and sparingly soluble in common organic solvents.

As is shown in Table 1 perfluoroheptadecan-9-one[5] was *ca.* four times as active as hexafluoroacetone in the epoxidation of cyclooctene with anhydrous H_2O_2[6] in refluxing EtOAc. Screening of several solvents revealed that polar, non-basic solvents, such as halogenated hydrocarbons and trifluoroethanol, were superior. Perfluoroheptadecan-9-one was only sparingly soluble in halogenated hydrocarbons. When 5 mol% was used it did not dissolve completely even in boiling 1,2-dichloroethane. Addition of 10 vol% of a cosolvent, *e.g.* EtOH or EtOAc, increased the solubility of the catalyst, resulting in a higher reaction rate. In this case the two requirements, anhydrous hydrogen peroxide and the need for a cosolvent, could be met by using hydrogen peroxide in EtOAc, easily prepared by azeotropic drying.[6]

Table 1 Epoxidation of cyclooctene with anhydrous H_2O_2 in EtOAc catalysed by perfluoroketones[a]

Catalyst	Initial rate mol mol^{-1} h^{-1}	Yield (%)[b]
$CF_3C(O)CF_3$	2.4	82
$C_6F_5C(O)CF_3$	1.3	74
$C_8F_{17}C(O)C_8F_{17}$	10	98

[a] Conditions: 5 mmol cyclooctene, 1 mmol n-decane (internal standard), 0.25 mmol perfluoroketone (5 mol%), 10 mmol H_2O_2 in 10 ml EtOAc. Reflux under N_2. Analysis by GC. [b] After 24 h.

Table 2 shows the results for epoxidation of several alkenes catalyzed by perfluoroheptadecan-9-one in refluxing 1,2-dichloroethane. Most epoxides are obtained in excellent yields, except for extremely acid-sensitive epoxides like camphene

Table 2 Epoxidation with anhydrous H_2O_2 in dichloroethane–EtOAc catalysed by perfluoroheptadecan-9-one[a]

Alkene	Initial rate/ mol mol^{-1} h^{-1}	*t*/h	Yield (%)
Cyclooctene	42	2	100
Cyclooctene[b]	41	2	96
Cyclooctene[c]	—	2	12
Cyclohexene	48	2	92
1-Methylcyclohexene	70	0.5	97
Methylenecyclohexane	15	2	64
Limonene	77	0.5	72
α-Pinene[d]	38	0.5	55
Camphene[d]	23	1.5	49
2-Methylundec-1-ene	28	1.5	96
Dec-1-ene	4.4	18	72

[a] Conditions: 5 mmol alkene, 1 mmol n-decane (internal standard), 0.25 mmol perfluoroheptadecan-9-one (5 mol%), 10 mmol H_2O_2 in 1 ml EtOAc and 10 ml 1,2-dichloroethane. Reflux under N_2. Analysis by GC. [b] 5 mol% of recovered catalyst was used. [c] No catalyst was added. [d] 5 mol% of Na_2HPO_4 was added.

Table 3 Epoxidation with 60% H_2O_2 in trifluoroethanol catalysed by perfluoroheptadecan-9-one[a]

Alkene	Initial rate/ mol mol^{-1} h^{-1}	*t*/h	Yield (%)
Cyclooctene	80	2	100
Cyclooctene[b]	82	2	100
Cyclooctene[c]	—	2	50
Cyclohexene[d]	34	1	64
1-Methylcyclohexene[d]	175	0.5	89
Methylenecyclohexane[d]	47	0.5	62
2-Methylundec-1-ene[d]	13	2	63
Dec-1-ene[d]	1.9	18	57

[a] Conditions: 5 mmol alkene, 1 mmol diglyme (internal standard), 0.25 mmol perfluoroheptadecan-9-one (5 mol%), 10 mmol H_2O_2 in 5 ml trifluoroethanol. Reflux under N_2. Analysis by GC. [b] 5 mol% of recovered catalyst was used. [c] No catalyst was added. [d] 5 mol% of Na_2HPO_4 was added.

oxide and α-pinene oxide. These epoxides can be obtained in moderate yields by buffering the reaction mixture with a small amount of base (Na_2HPO_4).

Simple cooling of the reaction mixture in an ice-bath (0 °C) gave crystallisation of the catalyst. Filtration and washing with a small amount of cold solvent gave the pure catalyst in about 80% yield. Quantitative GC measurements showed that the catalyst was not decomposed under the reaction conditions and was completely removed from the reaction mixture after filtration.‡ An interrupted catalytic experiment§ showed that no catalytically active material was present in the filtrate. A catalytic experiment on a larger scale (1 g of catalyst) gave a recovery of the catalyst of 92% after cooling to 0 °C and filtration. The recovered catalyst was still active in epoxidation with the same rates and yield.

The reaction could also be performed with 60% aqueous hydrogen peroxide in boiling trifluoroethanol. This solvent is known to be an excellent solvent in combination with aqueous hydrogen peroxide.[7] Table 3 shows the results for the epoxidation of several alkenes catalysed by perfluoroheptadecan-9-one in boiling trifluoroethanol. The yields are moderate to high, but the formation of acid-sensitive epoxides is only possible when the reaction medium is buffered by a phosphate buffer (*e.g.* 5 mol% of Na_2HPO_4). In this solvent simple cooling of the reaction mixture also resulted in crystallisation of the catalyst, but the recovery was generally lower than in dichloroethane. GC measurements indicated that a part of the catalyst remained dissolved in the reaction mixture after filtration.

We are currently investigating the scope of perfluoro ketones as catalysts for oxidations with hydrogen peroxide.

Notes and references

† Hexafluoroacetone is a gas. Perfluoroheptadecan-9-one is a solid with a melting point of 110 °C and an atmospheric boiling point of about 170 °C.

‡ The *ca.* 20% loss of the catalyst is attributed to losses incurred during sampling and mechanical losses associated with the small scale of the reactions (200 mg of catalyst).

§ A standard catalytic experiment was interrupted by cooling to 0 °C at 70% conversion. The catalyst was removed by filtration. The filtrate was again heated under reflux. The reaction proceeded but with a rate about 30 times lower; comparable to the blank reaction.

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