



## Novel epoxidation reaction of perfluoroalkenes with trimethylamine *N*-oxide and iodosylbenzene

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**Abstract**—Trimethylamine *N*-oxide and iodosylbenzene were found to be useful reagents for the epoxidation of tri- and tetra-substituted perfluoroalkenes in good to excellent yields. A catalytic epoxidation method was also developed by coupling this reaction with the *N*-oxidation of trimethylamine by hydrogen peroxide or perbenzoic acid. © 2002 Elsevier Science Ltd. All rights reserved.

Epoxides play an important role in fluorocarbon chemistry.<sup>1</sup> We previously reported<sup>2</sup> that *N,N*-diethylhydroxylamine (DEHA) epoxidizes highly branched perfluoroalkenes. With less branched perfluoroalkenes epoxidation competes poorly with simple nucleophilic addition. For example, perfluoro-2-methyl-2-pentene and DEHA form the addition product in high yield but no epoxide. In order to eliminate the addition pathway we examined reagents such as *N*-oxides, which have no acidic hydrogen. We found that trimethylamine *N*-oxide (TMNO) and iodosylbenzene epoxidize tri- and tetra-substituted perfluoroalkenes in good to excellent yields.

The epoxidation of perfluoroalkene **1** was tested using a variety of reagents and conditions summarized in Table 1. All reactions were conducted under heterogeneous two-phase conditions with vigorous stirring. The substrate perfluoroalkenes and the product epoxides form a bottom fluorine phase so that the products were readily isolated by separating the lower fluorine layer from the organic solvent layer containing the epoxidation reagents. Yields were calculated by gas chromatography using *trans*-perfluorodecalin as an internal standard. All epoxides produced in this article are known.<sup>3</sup>

As expected, electrophilic reagents such as hydrogen peroxide, trifluoroperacetic acid, and *meta*-chloroperbenzoic acid (MCPBA), which are commonly used for epoxidation in hydrocarbon chemistry, gave no reaction with the electrophilic<sup>4</sup> perfluoroalkenes (runs 1–3). However, the nucleophilic TMNO was able to epoxidize **1** to give a corresponding epoxide **2** in excellent yields. For example, a quantitative yield was obtained in DMF under mild conditions (30 min stirring at room temperature, run 4) and an 89% yield was obtained in water under more forcing conditions (3 days stirring at 60°C, run 5). Morpholine *N*-oxide (commercially available as a 50% (w/w) aqueous solution), which is a well-known<sup>5</sup> terminal co-oxidant for osmium tetroxide dihydroxylation of alkenes, is found less reactive than TMNO (runs 6–8). Almost no reaction was observed with morpholine *N*-oxide at room temperature (99% unchanged **1**, and 1% of **2**, run 6) and only 44% yield of **2** was obtained after 7 days stirring at 60°C (42% unchanged **1**; by-products in the water layer were not characterized, run 7). Pyridine *N*-oxide, which recently has been shown to be a useful terminal co-oxidant for the epoxidation of alkenes by Mn–Salen complexes,<sup>6</sup> gave no reaction with **1** (run 9). Although pyridine should be a better leaving group than trimethylamine, the pyridine *N*-oxide may not be a strong enough nucleophile to attack alkene **1** (on the reaction mechanism, vide infra). Triphenylphosphine oxide gave no reaction with **1** (run 10). Iodosylbenzene, which is also used as the terminal oxidant for the Mn–Salen epoxidation of alkenes,<sup>7</sup> reacted with **1** to give the epoxide **2** in quantitative yield (run 11). The previously known

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sodium hypochlorite epoxidation<sup>8</sup> is also included for comparison (run 12).

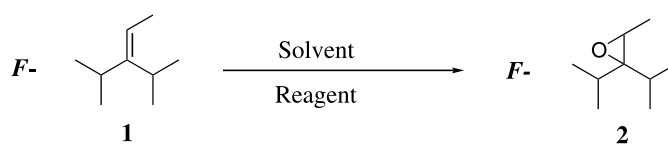
TMNO, which gave the best result in the reagent survey, was studied further with other perfluoroalkenes (Table 2). Perfluoroalkene **3** reacted with TMNO in DMF at a slower rate than **1** to give the corresponding epoxide in good yield (by-products in water layer were not characterized, run 1). Perfluoroalkene **4**, a less reactive double bond isomer of **1**, also reacted under the same reaction conditions with a slower rate to give the same epoxide **2** as in the case of **1** in nearly quantitative yield (run 3). The underlying reason for the formation of **2** is the same as reported previously in the epoxidation reaction of **4** with DEHA.<sup>1</sup> Equilibrium is established between alkenes **4** and **1** with the aid of a catalytic amount of fluoride ion produced by the attack of TMNO on **4**. The available alkene **1** is then epoxidized to **2** by the TMNO. When the reaction was conducted in water, neither **3** nor **4** reacted even at 60°C (runs 2 and 4). While perfluoroalkene **5** reacted violently with TMNO at room temperature to give a complicated mixture, the reaction was controlled by using lower temperatures (between –20 and –30°C) to give the corresponding epoxide in excellent yield (runs 5 and 6). The disubstituted perfluoroalkene **6** did not react under the same conditions (run 7).

Since trimethylamine is easily oxidized by MCPBA to the *N*-oxide<sup>9</sup> it is expected that a catalytic oxidation may proceed. The results are summarized in Table 3.

As expected, perfluoroalkene **1** was smoothly epoxidized by MCPBA in the presence of catalytic amount of trimethylamine at room temperature in DMF, giving the corresponding epoxide **2** in 96% conversion and yield (run 1). In run 2 it was demonstrated that only a slight excess of MCPBA was required. When acetonitrile was used as the solvent (run 3), a prolonged reaction time was necessary which resulted in a lower yield. Trimethylamine is indispensable for this epoxidation as is clear by run 3 of Table 1, in which no reaction occurred between **1** and MCPBA after 5 days under the same reaction conditions. A catalytic cycle for this epoxidation of perfluoroalkenes is shown in Scheme 1. Transfer of the highlighted oxygen to the perfluoroalkene is facilitated by an umpolung effect of transforming the electrophilic oxygen of MCPBA into the nucleophilic oxygen of TMNO. Run 4 of Table 3 shows that the less expensive urea–H<sub>2</sub>O<sub>2</sub> complex<sup>10</sup> is also usable as an oxidant source. The ready formation of TMNO by the reaction between trimethylamine and hydrogen peroxide has been known<sup>11</sup> so that TMNO is likely to play an oxygen carrying role, but its relevance to the reaction process is somewhat obscure in this case because the urea–H<sub>2</sub>O<sub>2</sub> complex itself is able to epoxidize **1** albeit at a much slower rate (run 5).

Nucleophilic epoxidation reactions are rare in hydrocarbon chemistry, but alkenes having an electron-withdrawing substituent like carbonyl or sulfoxide are known<sup>8</sup> to undergo epoxidation by HOO<sup>–</sup>. The reaction mechanism for this nucleophilic epoxidation is well

**Table 1.** Epoxidation of perfluoroalkene **1** with various reagents



*F*- denotes all unmarked bonds are to fluorines

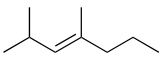
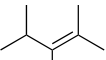
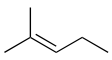
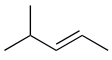
Run	Reagent	Quantity used	Solvent	Temp.	Time	Yield <sup>a</sup>
1	30% H <sub>2</sub> O <sub>2</sub>	Large excess	H <sub>2</sub> O	rt	3 days	N.R.
2	CF <sub>3</sub> CO <sub>3</sub> H	Large excess	H <sub>2</sub> O	rt	1 day	N.R.
3	MCPBA	1.0 equiv.	CH <sub>3</sub> CN	rt	5 days	N.R.
4	(CH <sub>3</sub> ) <sub>3</sub> NO	1.0 equiv.	DMF	rt	30 min	Quantit.
5		1.0 equiv.	H <sub>2</sub> O	60°C	3 days	89%
6		2.0 equiv.	H <sub>2</sub> O	rt	8 days	1%
7		2.0 equiv.	H <sub>2</sub> O	60°C	7 days	44%
8		2.0 equiv.	H <sub>2</sub> O	110°C	16 h	22%
9		1.5 equiv.	CH <sub>3</sub> CN	rt	2 h	N.R. <sup>b</sup>
10	Ph <sub>3</sub> PO	1.5 equiv.	DMF	rt	1 day	N.R.
11	PhIO	1.5 equiv.	DMF	rt	1 h	Quantit.
12	NaOCl <sup>c</sup>	1.5 equiv.	CH <sub>3</sub> CN	rt	15 h	Quantit.

<sup>a</sup> GC yields based on **1** used. Conversions for runs 7 and 8 are 58 and 38%, respectively. The others are 100%.

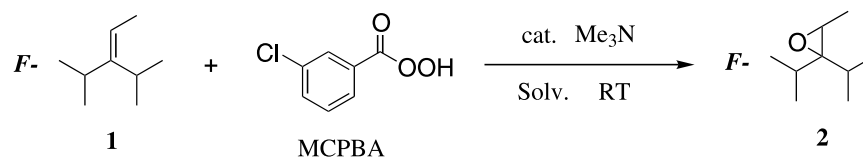
<sup>b</sup> N.R. = no reaction.

<sup>c</sup> An aqueous solution (2.5 M).

**Table 2.** Epoxidation of various perfluoroalkenes with 1.1 equiv. of trimethylamine *N*-oxide

Perfluoroalkenes		$(\text{CH}_3)_3\text{NO}$		Perfluoroepoxides	
		Solvent			
Run	Perfluoroalkenes	Solvent	Temp.	Time	Yield <sup>b</sup>
1	<i>F</i> - 	DMF	rt	2 h	63%
2	<b>3</b>	H <sub>2</sub> O	60°C	3 days	N.R.
3	<i>F</i> - 	DMF	rt	60 min.	97%
4	<b>4</b>	H <sub>2</sub> O	60°C	3 days	N.R.
5	<i>F</i> - 	DMF	rt	-	- <sup>c</sup>
6	<b>5</b>	DMF	-30°C	1 h	98%
7	<i>F</i> - 	DMF	-30°C	2 h	N.R.
	<b>6</b>				

<sup>a</sup> *F*- denotes all unmarked bonds are to fluorines. <sup>b</sup> GC yield (reactions were carried out until all the starting perfluoroalkenes are consumed) <sup>c</sup> Vigorous reaction occurred.  
N.R.: no reaction

**Table 3.** Epoxidation of the perfluoroalkene **1** by MCPBA or urea–H<sub>2</sub>O<sub>2</sub> with TMA catalyst

*F*- denotes all unmarked bonds are to fluorines

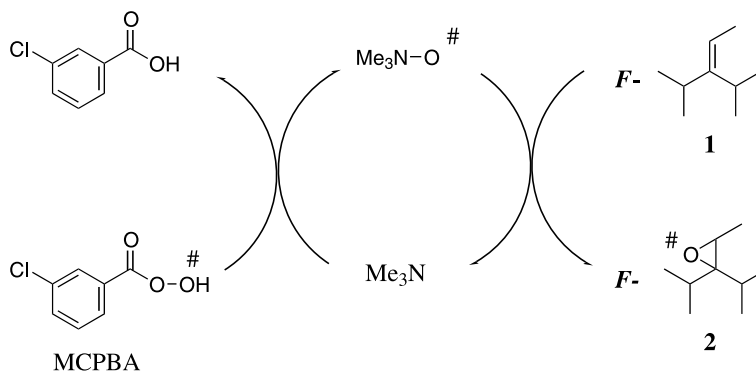
Run	Oxidant	Me <sub>3</sub> N <sup>a</sup>	Solv.	Time (h)	Conv. (%)	Yield <sup>b</sup> (%)
1	MCPBA	1.5 equiv.	DMF	1.0	96	96
2		1.1 equiv.	DMF	0.5	85	99
3		2.0 equiv.	CH <sub>3</sub> CN	2.5	68	86
4	Urea–H <sub>2</sub> O <sub>2</sub> complex	1.1 equiv.	DMF	30	75	81
5		1.1 equiv.	DMF	112	54	89

<sup>a</sup> 40 % aq. solution.

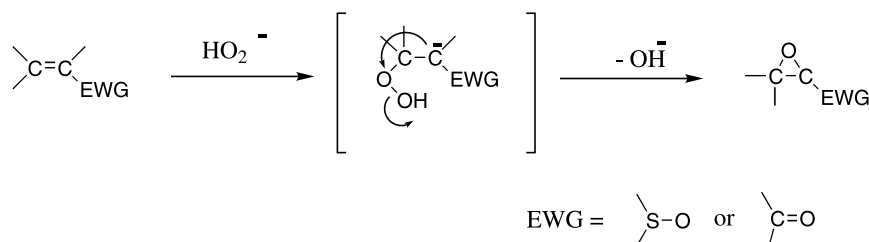
<sup>b</sup> Determined by GC based on **1** consumed.

established as shown in Scheme 2. The reaction mechanism of the epoxidation of perfluoroalkenes is analogously described in Scheme 3. Trimethylamine and iodobenzene are leaving groups corresponding to the OH<sup>−</sup> ion in Scheme 2. It seems to be worthwhile to note the easy elimination of trimethylamine from a quaternary trimethylammonium salt under mild basic conditions<sup>12</sup> for understanding the present mechanism (Scheme 4).

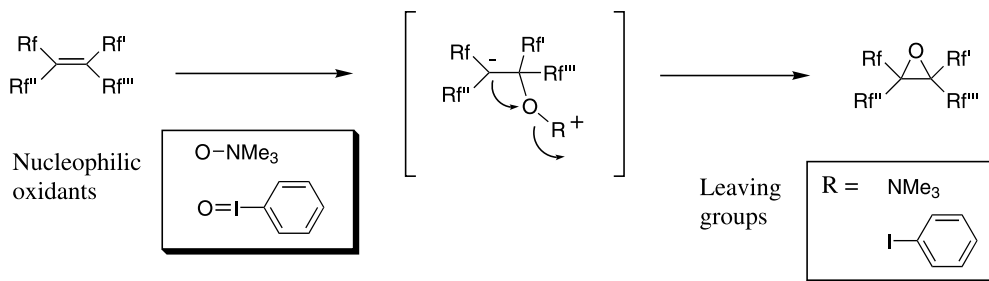
Thus, we have found that TMNO is a good epoxidation reagent for tri- and tetra-substituted perfluoroalkenes. Disubstituted perfluoroalkenes apparently are not sufficiently electrophilic for attack by TMNO. Furthermore, electrophilic epoxidation reagents such as MCPBA can be used for the reaction by using trimethylamine as a catalyst, with TMNO formed as an intermediate nucleophilic oxygen carrier between the two electrophilic substrates. The asymmetric epoxida-



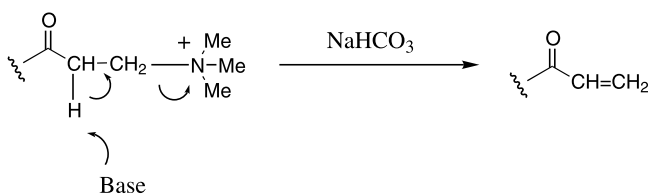
**Scheme 1.** A catalytic cycle for the epoxidation of **1**. The oxygen atom labeled # is transferred from MCPBA to **1** by trimethylamine through its conversion to *N*-oxide.



**Scheme 2.** Reaction mechanism on nucleophilic epoxidation of the alkenes conjugated with an electron-withdrawing group (EWA).



**Scheme 3.** Reaction mechanism of epoxidation of perfluoroalkenes with trimethylamine *N*-oxide and iodobenzene.



**Scheme 4.** Trimethylamine as a leaving group.

tion by using chiral amine *N*-oxides is under investigation.

#### Acknowledgements

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