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Methyltrioxorhenium-catalysed epoxidation of alkenes: enhancement of reactivity in hexafluoro-2-propanol

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Abstract—Methyltrioxorhenium-catalysed epoxidation of alkenes with hydrogen peroxide can be improved by using hexafluoro-2-propanol as a solvent. Quantitative conversions of cyclic and terminal olefins can be obtained with only 30% H_2O_2 and 0.1 mol% of catalyst. © 2002 Elsevier Science Ltd. All rights reserved.

In the course of our study on oxidation reactions in fluorous phase, we have reported that the activity of hydrogen peroxide is markedly increased when reactions are performed in fluorous alcohols, in particular in hexafluoroisopropanol (HFIP).[1] Neumann[2] and Sheldon[3] took advantage of such an activating effect for epoxidation reactions with H_2O_2 in HFIP without any catalyst. However, the use of 60% H_2O_2 at reflux is needed for good conversions, which is evidently a great drawback for a safe protocol.

Recently, it was published that with the addition of methyltrioxorhenium (MTO) as catalyst,[4] epoxidations in trifluoroethanol (TFE) could be efficiently performed at room temperature.[5] In comparison to reactions performed in CH_2Cl_2[6] the amount of catalyst could be reduced from 0.5 to 0.1 mol%. However, the protocol still requires the use of 60% hydrogen peroxide (two equivalents). Since HFIP is a better hydrogen bond donor ($\alpha = 1.96$) than TFE ($\alpha = 1.51$),[7] and a more dissociative one ($Y = 3.61$ and 1.80, respectively),[8] we tried to find mild conditions for epoxidation by combining the powerful catalyst MTO and HFIP as a strong activator of H_2O_2.

Before investigation of epoxidation reactions, the stability of HFIP in the MTO/H_2O_2 oxidative system, and the stability of the MTO/H_2O_2 catalyst in HFIP have been evaluated. In order to see whether HFIP can be oxidized in this system, we added 0.45 mL of 30% H_2O_2 into a solution of 10 mg of MTO (0.04 mmol) in 1 mL of HFIP. After 1 h stirring at room temperature, the ^{19}F NMR spectrum was recorded and only the signal of HFIP was observed. Further, stability of the peroxo form of MTO in HFIP and TFE was compared. MTO (1 mg) was dissolved in 2 mL of solvent, 1 mL of 30% H_2O_2 was added and the solution was stirred at room temperature. The yellow colour of the solution indicates the presence of the active form of catalyst. In TFE a colourless solution was obtained within 1 h, while in HFIP, the catalyst decomposed only after 6 h. A similar experiment was performed in the presence of pyrazole and the catalyst was active for 3 h in TFE and 10 h in HFIP.

After these verifications, we first investigated the epoxidation of cyclooctene using 2 equivalents of 30% H_2O_2, only 0.1 mol% of MTO as catalyst and 10 mol% of pyrazole as ligand at 0°C in different solvents. The conversion of the alkene into epoxide was followed by GC chromatography. As can be seen from Fig. 1, the epoxidation in CH_2Cl_2 was not complete after 4 h, while the reaction in trifluoroethanol (TFE) was easier and the oxirane was quantitatively formed after 4 h. When performed in HFIP, epoxidation was even faster than in TFE and complete conversion was obtained within 1 h.[9] This reaction time was obtained in TFE only with 60% H_2O_2.[5] In HFIP, a complete conversion could also be obtained with only 1.2 equivalent of 30% H_2O_2. We then explored the influence of added ligand. When reducing the amount of pyrazole to 5 mol%, conversion was also complete in 2 h; using only 1 mol% the epoxidation drastically decreased, confirming the role of the basic ligand not only on the acidity of the catalyst but also on its stability.[6a]

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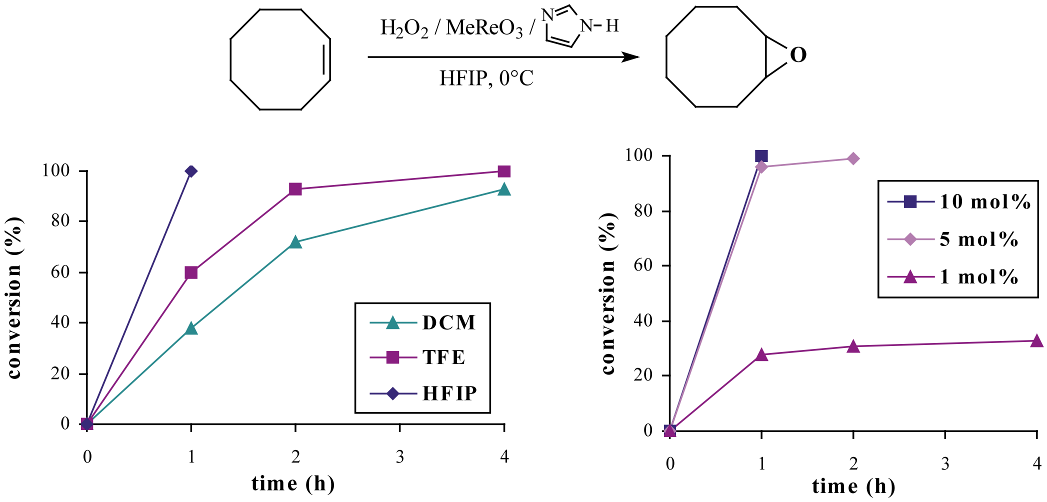
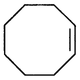
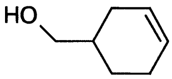
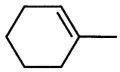
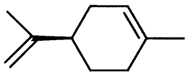
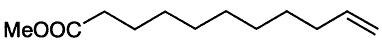
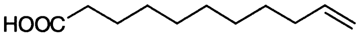
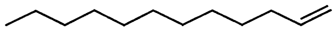


Figure 1. (left) The effect of solvent on epoxidation of cyclooctene: 4 mmol cyclooctene, 0.1 mol% MTO, 10 mol% pyrazole, 8 mmol 30% H_2O_2, 2 mL solvent, 0°C. (right) Reactions with different amounts of pyrazole in HFIP.

Having established that the use of HFIP as a solvent for the epoxidation with MTO/30%H_2O_2 system is very promising, we have extended its application to various key alkenes. Cyclic alkenes (cyclooctene, 1-(3-cyclohexene)methanol) were reactive and oxiranes were quantitatively formed within 1 h at 0°C (Table 1). However, with cyclic trisubstituted alkenes such as 1-methylcyclohexene and limonene, the catalyst decomposed (as indicated by disappearance of the yellow colour) and the epoxidation was not complete. Since the structure of MTO ligand plays an important role in the stability of the catalyst,[6a] we used 2,2′-bipyridine as a ligand instead of pyrazole for this two substrates.[10] This resulted in a quantitative conversion to the oxirane, again in 1 h at 0°C. The reaction of limonene occurred only at the cyclic double bond and diastereoisomers were formed in a 1.3:1 ratio (according to GC analysis). In the reaction with α-pinene, styrene and indene, all starting material was consumed; however, resulting epoxides were not stable during reaction. Despite the

Table 1. Epoxidation of alkenes by MTO/30% H_2O_2 in HFIP[a]

Entry	Substrate	Conditions	Conv.[b]	Isol. yield (%)
1		0°C, 1h	100%	93
2		〃	〃	89
3		〃[c]	〃	91
4		〃[c]	〃[d]	81
5		rt, 24h[e]	〃	88
6		rt, 6h	〃	80
7		rt, 24h[f]	93%	88

[a] Reaction conditions: 0.1 mol% MTO, 10mol% pyrazole, 2eq. 30% H_2O_2, 4mmol alkene in 2mL HFIP.

[b] Determined by NMR and GC analysis.

[c] 2,2'-bipyridine was used as additive.

[d] Only monoepoxide was formed.

[e] Suprisingly coulour is still yellow after 24h.

[f] Solvent: HFIP/BTF (1:1).

low nucleophilicity of HFIP, which can even be used as a solvent in oxirane ring-opening by nucleophiles,[11] these three acid-sensitive epoxides underwent the ring-opening leading to a mixture of compounds, as already observed in similar reactions.

Finally, reactivity of less reactive terminal aliphatic alkenes was assessed. The methyl ester of 1-undecen-10-oic acid was quantitatively converted into the corresponding epoxide with 0.1 mol% of MTO and 10 mol% of pyrazole at room temperature in 1 day. The presence of the free acid functionality is also compatible with this epoxidation method (entry 6, 6 h at room temperature).

Long chain terminal olefins, like 1-dodecene, are usually difficult to be epoxidized because of their low reactivity and their very poor solubility in polar solvents. Actually when 1-dodecene reacted with 30% H_2O_2 in HFIP in the presence of 0.1 mol% of MTO and 10 mol% of pyrazole, at room temperature, the conversion to 1-dodecene oxide was very low after 2 h of stirring and it did not increase with longer reaction time (Fig. 2). We tried to increase its solubility by the addition of dichloromethane (HFIP/CH_2Cl_2 = 3/1) but this resulted in the formation of a two-phase system and the yield was increased only to 21%. By the addition of trifluoromethylbenzene (BTF) to HFIP the reaction mixture became homogeneous; the reaction proceeded much better, and 93% of the epoxide was formed after 24 h of stirring at room temperature. Similar results were obtained using only half of the amount of pyrazole (5 mol%).

In conclusion, we have shown that the MTO/H_2O_2 system is very reactive in hexafluoroisopropanol. Epoxidation reactions are very efficient with 30% H_2O_2 at 0°C or room temperature, while in 1,1,1-trifluoroethanol 60% H_2O_2 was required for similar reactivity. Very little catalyst loading is needed (0.1 mol%). Furthermore, the use of a mixture of two fluorous solvents, a protic one (HFIP) and an aprotic one (trifluoromethylbenzene), allows the epoxidation of long unsaturated chains, including 1-dodecene by improving both, reactivity and solubility.

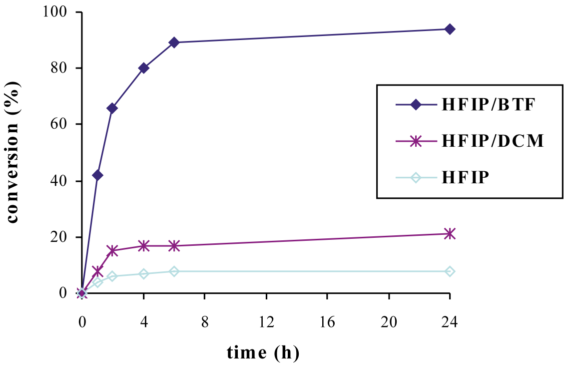


Figure 2. Epoxidation of 1-dodecene with MTO/H_2O_2: 4 mmol substrate, 0.1 mol% MTO, 10 mol% pyrazole, 8 mmol 30% H_2O_2, 2 mL solvent, rt.

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References

1. (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) Kesavan, V.; Bonnet-Delpon, D.; Bégué, J. P. *Synthesis* **2000**, 223–225; (d) Ravikumar, K. S.; Kesavan, V.; Crousse, B.; Bonnet-Delpon, D.; Bégué, J. P. *Org. Synth*., in press.
2. Neimann, K.; Neumann, R. *Org. Lett*. **2000**, *2*, 2861–2863.
3. van Vliet, M. C. A.; Ardens, I. W. C. E.; Sheldon, R. A. *Synlett* **2001**, 248–250.
4. Kühn, F. E.; Herrmann, W. A. *Chemtracts-Org. Chem*. **2001**, *14*, 59–83.
5. van Vliet, M. C. A.; Ardens, I. W. C. E.; Sheldon, R. A. *Chem. Commun*. **1999**, 821–822.
6. (a) Rudolph, J.; Reddy, K. L.; Chiang, J. P.; Sharpless, K. B. *J. Am. Chem. Soc*. **1997**, *119*, 6189–6190. Herrmann, W. A.; Ding, H.; Kratzer, R. M.; Kühn, F. E.; Haider, J. J.; Fisher, R. W. *J. Organomet. Chem*. **1997**, *549*, 319–322. Herrmann, W. A.; Kratzer, R. M.; Ding, H.; Thiel, W. R.; Glas, H. *J. Organomet. Chem*. **1998**, *555*, 293–295. Wang, W.-D.; Espenson, J. H. *J. Am. Chem. Soc*. **1998**, *120*, 11335–11341. Adolfsson, H.; Converso, A.; Sharpless, K. B. *Tetrahedron Lett*. **1999**, *40*, 3991–3994. Adolfsson, H.; Coperét, C.; Chiang, J. P.; Yudin, A. K. *J. Org. Chem*. **2000**, *65*, 8651–8658; (b) Coperét, C.; Adolfsson, H.; Sharpless, K. B. *Chem. Commun*. **1997**, 1565–1566. Boehlow, T. R.; Spilling, C. D. *Tetrahedron Lett*. **1996**, *37*, 2717–2720. Villa de P., A. L.; De Vos, D. E.; Montes de C., C.; Jacobs, P. A. *Tetrahedron Lett*. **1998**, *39*, 8521–8524; (c) Adam, W.; Saha-Möller, C. R.; Weichold, O. *J. Org. Chem*. **2000**, *65*, 2897–2899. Owens, G. S.; Abu-Omar, M. M. *Chem. Commun*. **2000**, 1165–1166. Vaino, A. R. *J. Org. Chem*. **2000**, *65*, 4210–4212. Yudin, A. K. Chiang, J. P.; Adolfsson, H.; Coperét, C. *J. Org. Chem*. **2001**, *66*, 4713–4718.
7. Kamlet, M. J.; Abboud, J.-L. M.; Abraham, M. H.; Taft, R. W. *J. Org. Chem*. **1983**, *48*, 2877–2887.
8. Schadt, F. L.; Bentley, T. W.; Schleyer, P.v. R. *J. Am. Chem. Soc*. **1976**, *98*, 7667–7674.
9. On preparative scale HFIP could be recovered by distillation.[1]
10. (a) Rudler, H.; Gregorio, J. R.; Denise, B.; Brégeault, J.-M.; Deloffre, A. *J. Mol. Cat. A* **1998**, *133*, 255–265; (b) Nakajima, M.; Sasaki, Y.; Iwamoto, H.; Hashimoto, S. *Tetrahedron Lett*. **1998**, *39*, 87–88.
11. (a) Kesavan, V.; Bonnet-Delpon, D.; Bégué, J. P. *Tetrahedron Lett*. **2000**, *41*, 2895–2898; (b) Das, U.; Crousse, B.; Kesavan, V.; Bonnet-Delpon, D.; Bégué, J. P. *J. Org. Chem*. **2000**, *65*, 6749–6751; (c) Rodrigues, I.; Bonnet-Delpon, D.; Bégué, J. P. *J. Org. Chem*. **2001**, *66*, 2098–2103; (d) Iskra, J.; Bonnet-Delpon, D.; Bégué, J. P., unpublished results.