SYNLETT Spotlight 223

Methy(trifluoromethyl)dioxirane (TFD): A Powerful and Versatile Oxidant in Organic Synthesis

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This feature focuses on a reagent chosen by a postgraduate, highlighting the uses and preparation of the reagent in current research

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Introduction

During the last two decades, the use of dioxiranes as oxidants in organic synthesis has increased considerably.¹ Methyl(trifluoromethyl)dioxirane (TFD) has the highest reactivity among dioxiranes reported so far, and has been utilized for a broad variety of oxidative transformations in organic synthesis. Exemplary transformations are the monohydroxylation of alkanes,² chemoselective oxidation of allylic alcohols,³ optically active *sec,sec*-1,2-diols⁴ and simple sulfides,⁵ oxyfunctionalization of unactivated tertiary and secondary C–H bonds of alkylamines⁶ and aliphatic esters,⁷ epoxidation of primary and secondary alkenylammonium salts⁸ and chiral camphor *N*-enoylpyrazolidinones,⁹ oxidative cleavage of acetals, ketals¹⁰ and aryl oxazolines,¹¹ and conversion of cyclic ethers into lactones.¹⁰ It is also found to be a useful reagent for the oxyfunctionalization of natural^{12–14} and non-natural^{15–19} targets, which include the direct hydroxylation at the side-chain C-25 of cholestane derivatives and vitamin D₃ Windaus–Grundmann ketone,¹² high stereo- and regioselective conversion of vitamin D₂ into its (*all-R*) tet-

raepoxide and C-25 hydroxy derivative,¹³ stereoselective synthesis of (*all-R*)-vitamin D₃ triepoxide and its 25-hydroxy derivative,¹⁴ oxidation of centropolyindans,¹⁵ buckminsterfullerene C₆₀,¹⁶ Binor S,¹⁷ hydrocarbons bearing cyclopropyl moieties,¹⁸ and selective bridgehead dihydroxylation of fenestrindane.¹⁹

Preparation

TFD can be readily prepared by the oxidation of 1,1,1-trifluoro-2-propanone with potassium peroxomonosulfate triple salt KHSO₅·KHSO₄·K₂SO₄ (Oxone®, Scheme 1). A dilute solution of TFD in 1,1,1-trifluoro-2-propanone with variable concentrations of 0.05–0.8 M or a ketone-free solution of TFD can be obtained and used in oxidative reactions.²⁰

Scheme 1

Abstracts

(A) *Oxyfunctionalization of Saturated Hydrocarbons*: A convenient application of TFD in organic synthesis is the direct oxyfunctionalization of saturated hydrocarbons.²¹ In this reaction, high selectivities were recorded for an oxygen insertion at the tertiary > secondary >> primary 'unactivated' C–H bonds. The oxidation of tertiary C–H gave tertiary alcohols, while oxidation of secondary carbons yielded primarily ketones.

(B) *Conversion of Alcohols into Carbonyl Compounds*: An efficient procedure for the oxidation of secondary alcohols to ketones is achieved using TFD as oxidant. Primary alcohols are converted into mixtures of aldehydes and acids.^{22a} Direct conversion of epoxy alcohols into epoxy ketones has also been achieved in high yield using this reagent.^{22b}

(C) *Epoxidation of Olefins*: TFD can be applied as a powerful oxidizing reagent for unfunctionalized, strongly electron-deficient, and electron-rich olefins under neutral reaction conditions.²³

(D) *Selective Oxidation of Acetylenic 1,4-Diols*: Curci and co-workers²⁴ showed that acetylenic 1,4-diols can be selectively oxidized to diketones by using TFD in acetone. When the free OH functionalities are masked by conversion into acetoxy, oxidation at the C≡C bond takes place instead.

(E) *Oxidative Cleavage of *p*-Methoxybenzyl Ethers*: TFD is also used for oxidative cleavage of the *p*-methoxybenzyl group to give the *E,Z*-configured aldehydo ester in aqueous acetonitrile.²⁵ The free hydroxyl, ester and amide groups, ketone and ether functionalities tolerate the oxidative ring-cleavage conditions.

(F) *Oxidation of Peptides*: Rella and Williard reported that Boc-protected and acetyl-protected peptide methyl esters bearing alkyl side chains undergo chemoselective oxidation using TFD under mild conditions. N-Hydroxylation took place in the case of the Boc-protected peptides, and side-chain hydroxylation occurred in the case of acetyl-protected peptides.²⁶

References

- (1) (a) Adam, W.; Curci, R.; Edwards, J. O. *Acc. Chem. Res.* **1989**, *22*, 205. (b) Curci, R.; D'Accolti, L.; Fusco, C. *Acc. Chem. Res.* **2006**, *39*, 1. (c) Murray, R. W. *Chem. Rev.* **1989**, *89*, 1187.
- (2) Asebsio, G.; Mello, R.; González-Núñez, M. E.; Castellano, G.; Corral, J. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 217.
- (3) (a) Adam, W.; Paredes, R.; Smerz, A. K.; Veloza, L. A. *Eur. J. Org. Chem.* **1998**, 349. (b) D'Accolti, L.; Fiorentino, M.; Fusco, C.; Rosa, A. M.; Curci, R. *Tetrahedron Lett.* **1999**, *40*, 8023.
- (4) D'Accolti, L.; Detomaso, A.; Fusco, C.; Rosa, A.; Curci, R. *J. Org. Chem.* **1993**, *58*, 3600.
- (5) Asensio, G.; Mello, R.; González-Núñez, M. E. *Tetrahedron Lett.* **1996**, *37*, 2299.
- (6) Asensio, G.; González-Núñez, M. E.; Bernardini, C. B.; Mello, R.; Adam, W. *J. Am. Chem. Soc.* **1993**, *115*, 7250.
- (7) Asensio, G.; Castellano, G.; Mello, R.; González-Núñez, M. E. *J. Org. Chem.* **1996**, *61*, 5564.
- (8) Asensio, G.; Mello, R.; Boix-Bernardini, C.; González-Núñez, M. E.; Castellano, G. *J. Org. Chem.* **1995**, *60*, 3692.
- (9) Fan, C. L.; Lee, W.-D.; Teng, N.-W.; Sun, Y.-C.; Chen, K. *J. Org. Chem.* **2003**, *68*, 9816.
- (10) Voigt, B.; Porzel, A.; Golsch, D.; Adam, W.; Adam, G. *Tetrahedron* **1996**, *52*, 10653.
- (11) Yang, D.; Yip, Y.-C.; Wang, X.-C. *Tetrahedron Lett.* **1997**, *38*, 7083.
- (12) Bovicelli, P.; Lupattelli, P.; Mincione, E. *J. Org. Chem.* **1992**, *57*, 5052.
- (13) Curci, R.; Detomaso, A.; Lattanzio, M. E.; Carpenter, G. B. *J. Am. Chem. Soc.* **1996**, *118*, 11089.
- (14) Curci, R.; Detomaso, A.; Prencipe, T.; Carpenter, G. B. *J. Am. Chem. Soc.* **1994**, *116*, 8112.
- (15) Kuck, D.; Schuster, A.; Fusco, C.; Fiorentino, M.; Curci, R. *J. Am. Chem. Soc.* **1994**, *116*, 2375.
- (16) Fusco, C.; Seraglia, R.; Curci, R. *J. Org. Chem.* **1999**, *64*, 8363.
- (17) D'Accolti, L.; Fusco, C.; Lucchini, V.; Carpenter, G. B.; Curci, R. *J. Org. Chem.* **2001**, *66*, 9063.
- (18) D'Accolti, L.; Dinoi, A.; Fusco, C.; Curci, R. *J. Org. Chem.* **2003**, *68*, 7806.
- (19) Fusco, C.; Fiorentino, M.; Dinoi, A.; Curci, R. *J. Org. Chem.* **1996**, *61*, 8681.
- (20) (a) Mello, R.; Fiorentino, M.; Sciacovelli, O.; Curci, R. *J. Org. Chem.* **1988**, *53*, 3890. (b) Mello, R.; González-Núñez, M. E.; Asensio, G. *Synlett* **2007**, 47.
- (21) (a) Mello, R.; Fiorentino, M.; Fusco, C.; Curci, R. *J. Am. Chem. Soc.* **1989**, *111*, 6749. (b) González-Núñez, M. E.; Royo, J.; Mello, R.; Báguena, M.; Ferrer, J. M.; de Arellano, C. R.; Asensio, G.; Prakash, G. K. S. *J. Org. Chem.* **2005**, *70*, 7919. (c) D'Accolti, L.; Fiorentino, M.; Fusco, C.; Capitelli, F.; Curci, R. *Tetrahedron Lett.* **2007**, *48*, 3575.
- (22) (a) Mello, R.; Cassidei, L.; Fiorentino, M.; Fusco, C.; Hümmel, W.; Jäger, V.; Curci, R. *J. Am. Chem. Soc.* **1991**, *113*, 2205. (b) D'Accolti, L.; Fusco, C.; Annese, C.; Rella, M. R.; Turteltaub, J. S.; Williard, P. G.; Curci, R. *J. Org. Chem.* **2004**, *69*, 8510.
- (23) Yang, D.; Wong, M.-K.; Yip, Y.-C. *J. Org. Chem.* **1995**, *60*, 3887.
- (24) D'Accolti, L.; Fiorentino, M.; Fusco, C.; Crupi, P.; Curci, R. *Tetrahedron Lett.* **2004**, *45*, 8575.
- (25) Paquette, L. A.; Kreilein, M. M.; Bedore, M. W.; Friedrich, D. *Org. Lett.* **2005**, *7*, 4665.
- (26) Rella, M. R.; Williard, P. G. *J. Org. Chem.* **2007**, *72*, 525.