

SYNLETT Spotlight 223

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



Compiled by Xu-Ye Tao

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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

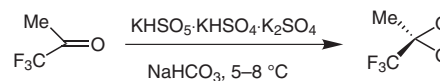
Introduction

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

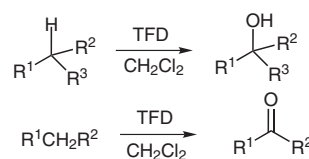
TFD can be readily prepared by the oxidation of 1,1,1-trifluoro-2-propanone with potassium peroxomonosulfate triple salt KHSO₅KHSO₄K₂SO₄ (Oxone[®], Scheme 1). A dilute solution of TFD in 1,1,1-trifluoro-2-propanone with variable concentrations of 0.05–0.8 M or a ketone-free solution of TFD can be obtained and used in oxidative reactions.²⁰



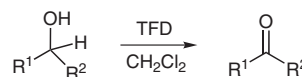
Scheme 1

Abstracts

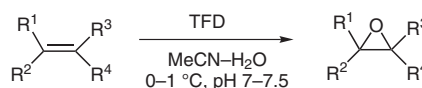
(A) *Oxyfunctionalization of Saturated Hydrocarbons*: A convenient application of TFD in organic synthesis is the direct oxyfunctionalization of saturated hydrocarbons.²¹ In this reaction, high selectivities were recorded for an oxygen insertion at the tertiary > secondary >> primary 'unactivated' C–H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



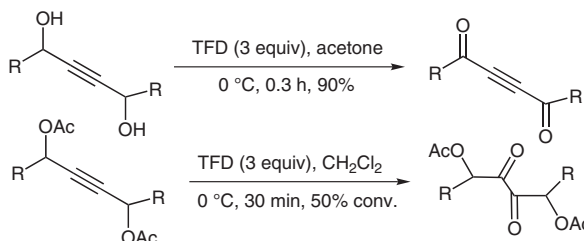
(B) *Conversion of Alcohols into Carbonyl Compounds*: An efficient procedure for the oxidation of secondary alcohols to ketones is achieved using TFD as oxidant. Primary alcohols are converted into mixtures of aldehydes and acids.^{22a} Direct conversion of epoxy alcohols into epoxy ketones has also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



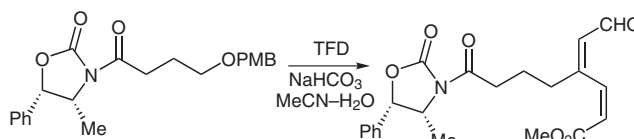
(C) *Epoxidation of Olefins*: TFD can be applied as a powerful oxidizing reagent for unfunctionalized, strongly electron-deficient, and electron-rich olefins under neutral reaction conditions.²³



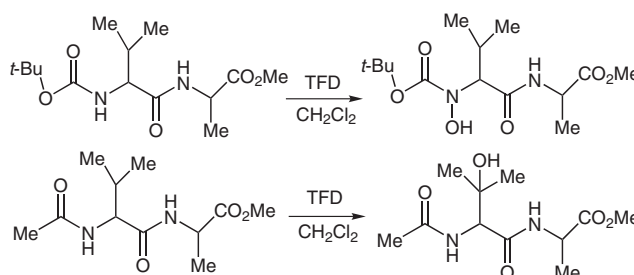
(D) *Selective Oxidation of Acetylenic 1,4-Diols*: Curci and co-workers²⁴ showed that acetylenic 1,4-diols can be selectively oxidized to diketones by using TFD in acetone. When the free OH functionalities are masked by conversion into acetoxy, oxidation at the $C\equiv C$ bond takes place instead.



(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



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