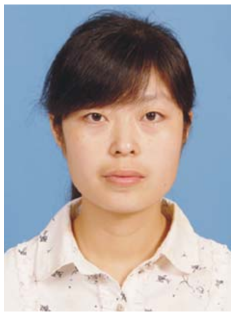
SYNLETT
Spotlight 223

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

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

Compiled by Xu-Ye Tao



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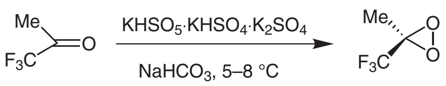
Introduction

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-diols[4] and simple sulfides,[5] oxyfunctionalization of unactivated tertiary and secondary C–H bonds of alkylamines[6] and aliphatic esters,[7] epoxidation of primary and secondary alkenylammonium salts[8] and chiral camphor *N*-enoylpyrazolidinones,[9] oxidative cleavage of acetals, ketals[10] 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 D_3 Windaus–Grundmann ketone,[12] high stereo- and regioselective conversion of vitamin D_2 into its (*all-R*) tetraepoxide and C-25 hydroxy derivative,[13] stereoselective synthesis of (*all-R*)-vitamin D_3 triepoxide and its 25-hydroxy derivative,[14] oxidation of centropolyindans,[15] buckminsterfullerene C_{60},[16] Binor S,[17] hydrocarbons bearing cyclopropyl moieties,[18] and selective bridgehead dihydroxylation of fenestrindane.[19]

Preparation

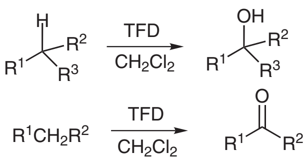
TFD can be readily prepared by the oxidation of 1,1,1-trifluoro-2-propanone with potassium peroxomonosulfate triple salt $KHSO_5KHSO_4K_2SO_4$ (Oxone®, Scheme 1). A dilute solution of TFD in 1,1,1-trifluoro-2-propanone with variable concentrations of 0.05–0.8 M or a ketone-free solution of TFD can be obtained and used in oxidative reactions.[20]



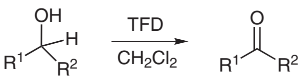
Scheme 1

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]



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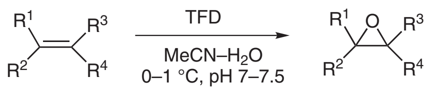
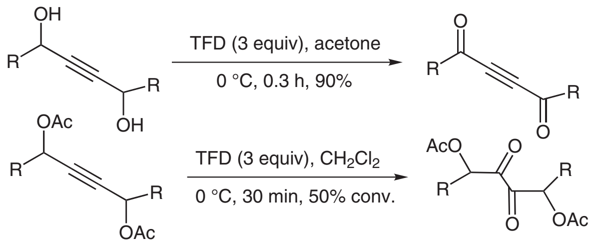
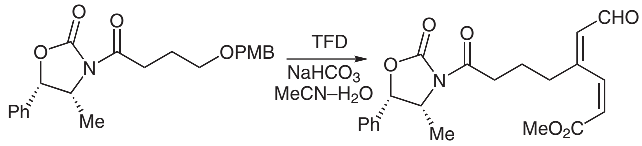
(C) *Epxoxidation of Olefins*: TFD can be applied as a powerful oxidizing reagent for unfunctionalized, strongly electron-deficient, and electron-rich olefins under neutral reaction conditions.[23]



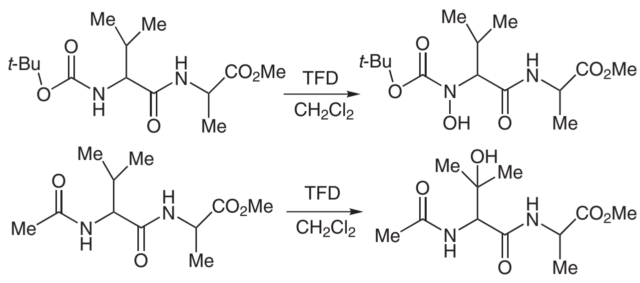
(D) *Selective Oxidation of Acetylenic 1,4-Diols*: Curci and coworkers[24] showed that acetylenic 1,4-diols can be selectively oxidized to diketones by using TFD in acetone. When the free OH functionalities are masked by conversion into acetoxy, oxidation at the C≡C bond takes place instead.



(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]



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