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Spotlight 271

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

Martin Sulfurane – A Versatile Reagent for Organic Synthesis

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Introduction

Martin Sulfurane, a diphenylsulfur compound, has been a versatile reagent in organic synthesis since the 1970s.

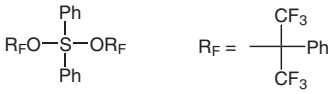
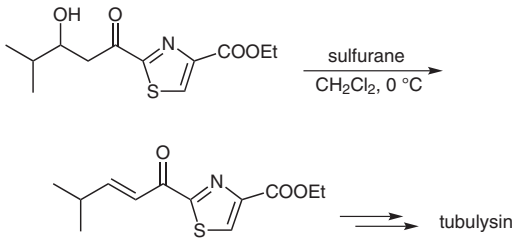


Figure 1

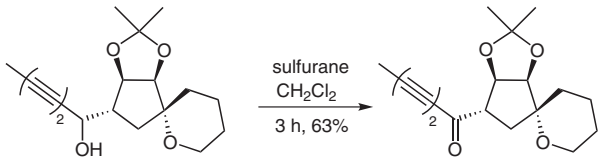
The Sulfurane is reactive towards active hydrogen compounds and is one of the reagents of choice for a class of reactions including dehydration, amide cleavage, epoxide formation, sulfinimine synthesis, oxidation and coupling.[1] The Martine Sulfurane has been prepared from hexafluoro-2-phenyl-2-propanol using KOH, diphenylsulfide and bromine.[1] The general mechanism of action involves the rapid exchange of one of the alkoxy ligands on the sulfurane, followed by ionisation giving an alkoxysulfonium ion, which, in turn, undergoes E1 or E2 elimination.[2] Since Martin Sulfurane is a mild and neutral reagent, these reactions are quite compatible with a wide range of functional groups like carbamate, carbonyl, ester, ether, etc. The reagent is applicable to the synthesis of many natural products.

Abstracts

(A) The dehydration of hydroxy compounds is an important strategy leading to the formation of enones, which are synthetically important precursors. This methodology was extended in our laboratory for the synthesis of tubulysins[3] following a series of synthetic transformations. The reaction was feasible even in presence of the thiazole moiety; the methodology being quite efficient for the synthesis of α,β-unsaturated carbonyl compounds from β-hydroxy ketones. Nicolaou et al. used the Martin Sulfurane mediated dehydration in the asymmetric total synthesis of platencin.[4]



(B) Under treatment with Martin Sulfurane some secondary alcohols underwent oxidation giving ketones. Koviach and co-workers reported an unusual oxidation during their studies directed to the synthesis of spiroketal enol ethers.[5] The proposed mechanism involved an intermediate similar to the alkoxysulfonium ion formed during DMSO-based oxidations like Swern oxidation, giving the product through an intramolecular deprotonation by R_FO^-.



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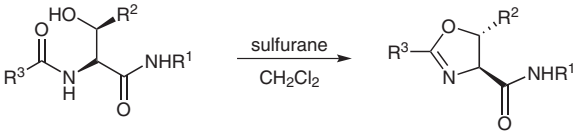
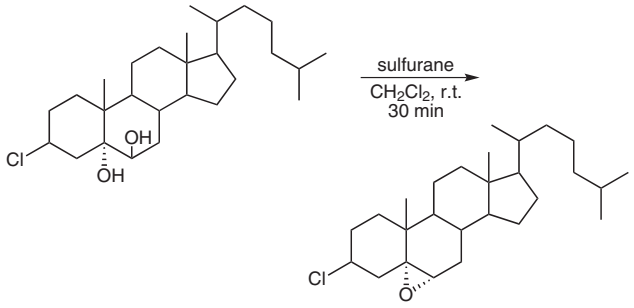
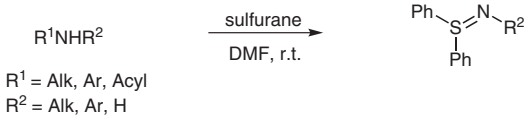
(C) Martin Sulfurane is a useful reagent for the cyclodehydration of *erythro*-*N*-acetyl-β-hydroxy-α-amino amides and dehydrative elimination of *threo*-β-hydroxy-α-amino acid derivatives. Thus, cyclodehydration of (2*R*,3*S*)-2-acetamido-3-hydroxybutanamides with Martin Sulfurane afforded 4,5-dihydrooxazoles.[6] The (2*R*,3*R*)-analogue underwent the normal dehydration reaction.



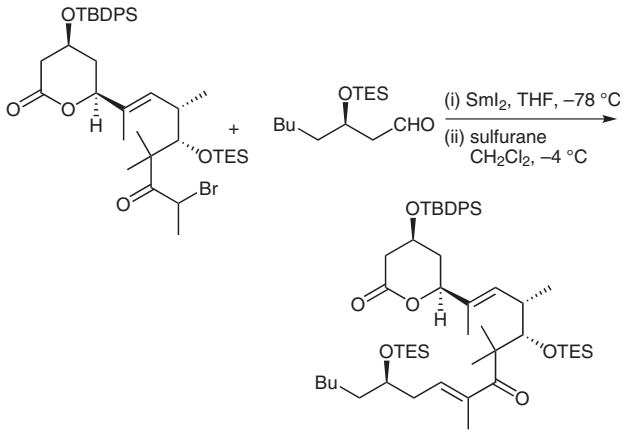
(D) Martin and co-workers reported the formation of cyclic ethers (epoxides) from 1,2-diols when treated with the sulfurane.[7] For instance, chlorocholestane diol gave the corresponding epoxide by the elimination of the secondary hydroxy group. The scope of the reaction could be extended to the synthesis of larger cyclic ethers by using longer chain diols. Thus 1,3-, 1,4- and 1,5-diols gave oxetanes, tetrahydrofurans and tetrahydropyrans, along with their open chain analogues and elimination products.



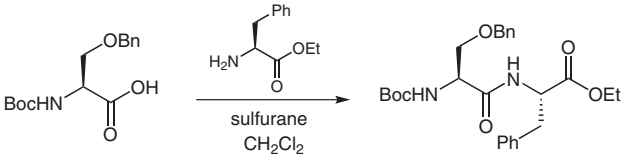
(E) Alkyl or aryl substituted primary amines, primary amides, sulfonamides and ammonia were reported to undergo oxidation on treatment with Martin Sulfurane.[8] Secondary amides in DMF underwent cleavage when treated with Martin Sulfurane leading to the formation of *S*,*S*-diaryl-*N*-alkyl sulfinimines,[9] which are of immense significance as they possess a remarkably reactive functional group centered at the S–N bond. The N-substituted sulfinimine products thus formed, through the rapid ligand-exchange reaction are of excellent synthetic utility.



(F) Martin Sulfurane was used by Jamison in the total synthesis of acutiphycin[10] in a two step procedure involving an unusual intermolecular Reformatsky reaction followed by dehydration with an overall yield of 72%. The α-quarternary center on the starting substrate prevented the side reactions of the samarium enolate and when coupled with subsequent dehydration using Martin Sulfurane, the two-step sequence is complementary to Horner–Wadsworth–Emmons strategies and may find use in similar sterically hindered systems.



(G) Yeheskiely and co-workers have reported coupling (amide bond formation) reactions between amino acids mediated by Martin Sulfurane in the absence of an external base.[11] The reaction facilitated rapid amide bond formation between N^{α}-urethane protected-L-amino acids in high yields and with no detectable racemization. This reaction can hence be employed in racemization sensitive systems such as segment condensations.



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