

SYNLETT Spotlight 214

Thionyl Chloride – A Versatile Reagent

Compiled by Mingdong Li



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

Mingdong Li was born in Jiangxi, P. R. of China. He completed his M.Sc. in medicinal chemistry at China Pharmaceutical University, Nanjing, in 2004. In the same year, he joined the Southeast University, Nanjing, where he is currently working towards his Ph.D. under the supervision of Dr. Min Ji. His research targets mainly tyrosine kinases inhibitor synthesis and new synthetic methods for the synthesis of nitrogen heterocycles.

Institute of Pharmaceutical Engineering School of Chemistry and Chemical Engineering, Jiangsu Laboratory for Biomaterials and Devices, Southeast University, 210096 Nanjing, P. R. of China
E-mail: seu301@126.com

Introduction

Thionyl chloride exhibits several features which have made it particularly attractive as a reagent in organic synthesis. It is often applied as a powerful chlorinating reagent, and reacts as such with carbonyl compounds, aromatic sulfochlorides, and aliphatic alcohols; the formed intermediates can be further transformed to other useful compounds.¹ It can also be used as an HCl precursor and reacts in electrophilic additions or substitutions with compounds containing C–C multiple bonds. Thionyl chloride also reacts with amines or imines to form sulfinyl chlorides and it reacts with active methyl or active methylene compounds to form sulfenyl chlorides through Pummerer-type rearrangement.² In addition, it can also be used as a chlorinating reagent through its oxidation and partial dehydrogenation of organic compounds to give

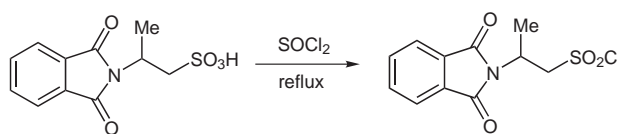
sulfonyl chloride. In some reactions it serves as condensing reagent to form heterocyclic compounds, or it can be used as catalyst.

In industrial production, thionyl chloride is used for the synthesis of carboxylic acid chlorides. These products are frequently used as intermediates for the production of pharmaceutical active ingredients, crop protection reagents, and dyestuffs.

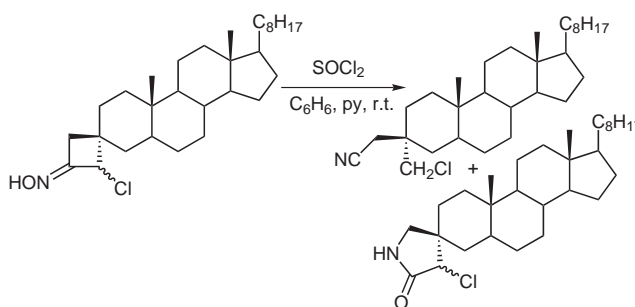
Compared with other chlorinating reagents, thionyl chloride has many advantages: The end product is easy to isolate, it is comparatively easy to handle, and the yields are generally high. It is miscible with nearly all organic solvents and is itself a good solvent for most organic compounds.

Abstracts

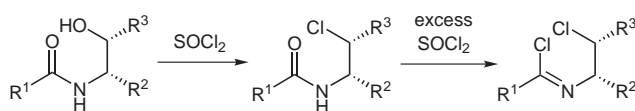
(A) Thionyl chloride is a powerful chlorinating reagent. It reacts with most carbonyl or aromatic sulfoacid compounds to give carboxylic acids or aromatic sulfochlorides, respectively.^{3,4}



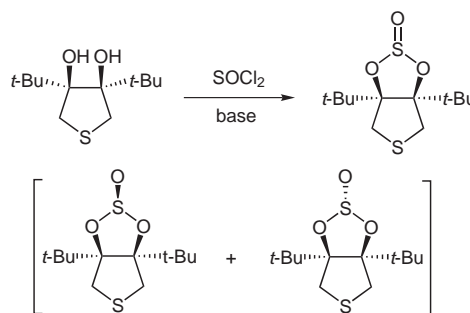
(B) A monochloroxime steroid reacts with thionyl chloride in the presence of pyridine traces in benzene via an abnormal Beckmann rearrangement.⁵



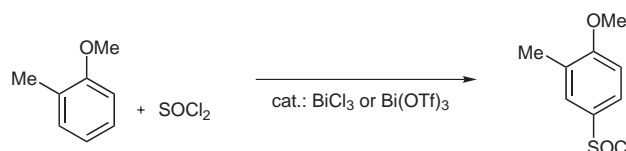
(C) Chlorination of amino alcohols with thionyl chloride gives chloroethyl amides; if excess thionyl chloride is used, the reaction yields chloroethyl imidoyl chlorides.⁶



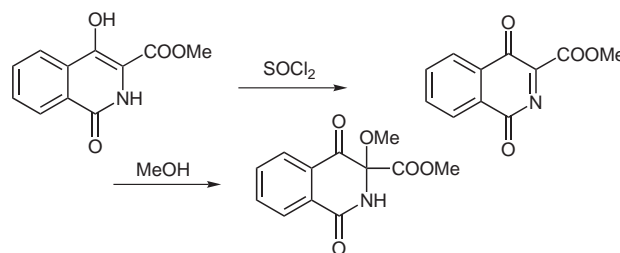
(D) *Ortho*-diols react with thionyl chloride to give sulfites (a mixture of two diastereomers) in excellent combined yields.⁷



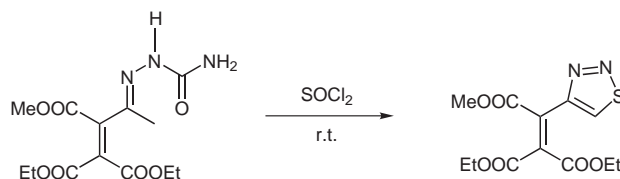
(E) In the presence of a Lewis acid catalyst, 2-methylanisole reacts with SOCl_2 in a Friedel–Crafts reaction, which yields the corresponding aryl sulfinyl chloride.⁸



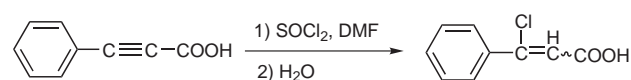
(F) Thionyl chloride can also be used as a chlorinating agent through its oxidation and partial dehydrogenation of organic compounds.⁹



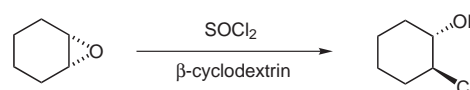
(G) Thionyl chloride is also used as a cyclization reagent to synthesize heterocyclic compounds.^{10,11}



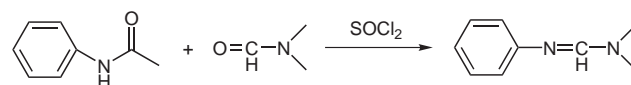
(H) Thionyl chloride can be used as an HCl precursor and reacts with compounds containing $\text{C}-\text{C}$ multiple bonds.¹²



(I) (1*R*,6*S*)-7-oxabicyclo[4.1.0]heptane was regioselectively ring-opened under supramolecular catalysis conditions to afford (1*S*,2*S*)-2-chlorocyclohexanol.¹³



(J) Thionyl chloride also serves as condensing agent.¹⁴



References

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