Oxalyl Chloride: A Versatile Reagent in Organic Synthesis

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Introduction

Oxalyl chloride is a very versatile reagent extensively used by organic chemists. One of its most common uses is in oxidation of alcohols to aldehydes and ketones named Swern oxidation.\(^1\)\(^-\)\(^5\) However, this reagent can efficiently be applied in many other reactions such as 1,1-cycloadditions with 1,4-dilithio-1,3-dienes or zirconacyclopentadienes,\(^6\) cyclization of 1,3-bis(trimethylsilyl)alk-1-ynes to isoeletronic acids,\(^7\) preparation of phenyl isocyanates from anilines,\(^8\) bicyclization of biaryl acetamides,\(^9\) dehydration of formamides to afford nitriles,\(^10\) and cyclization of 1,1-bis(trimethylsilyl)ketene acetals to give 3-hydroxymaleic anhydrides.\(^11\)

Abstracts

(A) He and Chan showed a new class of odorless and non-volatile organosulfur compounds anchored on imidazolium ionic liquid, which can be used effectively for the oxidation of alcohols to aldehydes and ketones in the presence of oxalyl chloride\(^1\) under Swern oxidation conditions.\(^2\)

\[
\begin{align*}
\text{Oxalyl chloride} + \text{alcohol} &\rightarrow \text{aldehyde or ketone} \\
1) (\text{COCl})_2 &\rightarrow \text{aldehyde} \\
2) \text{Et}_3\text{N} &\rightarrow \text{aldehyde} \\
\end{align*}
\]

(B) Chen and workgroup reported a 1,1-cycloaddition of oxalyl chloride with 1,4-dilithio-1,3-dienes or zirconacyclopentadienes in the presence of CuCl and DMPU to afford cyclopentadienone derivatives in good yields.\(^6\)

\[
\begin{align*}
\text{Oxalyl chloride} + \text{zirconacyclopentadiene} &\rightarrow \text{cyclopentadienone} \\
\text{CuCl} &\rightarrow \text{CuCl} \\
\text{DMPU, 0 °C, 1 h} &\rightarrow \text{cyclopentadienone} \\
\end{align*}
\]
(C) Dede et al. showed a regioselective preparation of isoeletronic acids by cyclization of 1,3-bis(trimethylsilyloxy)alk-1-enes with oxalyl chloride in moderate yields.\(^7\)

\[
\begin{align*}
\text{R}^1\text{SiOSiMe}_3\text{R}^2 & \xrightarrow{\text{MeSiOTf (0.5 equiv), (COCl)}_2} \text{R}^1\text{R}^2\text{R}^3\text{R}^4\text{R}^5\text{N} & \xrightarrow{\Delta (130-140 \degree \text{C}), 2-3 \text{ h}} \text{R}^1\text{R}^2\text{R}^3\text{R}^4\text{R}^5\text{CONH} \\
\text{R}^1 = \text{Et}, \text{R}^2 = \text{OEt} (77\%) & \text{R}^1 = \text{nPr}, \text{R}^2 = \text{OEt} (71\%) & \text{R}^1 = \text{nBu}, \text{R}^2 = \text{OEt} (75\%)
\end{align*}
\]

(D) Oh et al. reported a new and convenient method of generating phenyl isocyanates from anilines using oxalyl chloride. Aylation of a variety of substituted aniline hydrochlorides with oxalyl chloride affords the intermediate oxamic chlorides, which smoothly undergo thermal decomposition to the corresponding desired products.\(^8\)

\[
\begin{align*}
\text{R}^1\text{NHR} & \xrightarrow{\text{MeOH}} \text{R}^1\text{NR}^2 & \text{R}^1 = \text{R}^2 = \text{R}^4 = \text{R}^5 = \text{H} (85\%) & \text{R}^1 = \text{OMe}, \text{R}^2 = \text{R}^3 = \text{R}^4 = \text{R}^5 = \text{H} (81\%) & \text{R}^1 = \text{R}^2 = \text{R}^4 = \text{R}^5 = \text{H}, \text{R}^3 = \text{SMe} (98\%) & \text{R}^1 = \text{R}^2 = \text{R}^4 = \text{R}^5 = \text{H}, \text{R}^3 = \text{NO}_2 (98\%)
\end{align*}
\]

(E) Suau et al. showed that oxalyl chloride is a good promoter for bicyclization of a variety of biarylactamides in the presence of SnCl\(_4\), which were used for the synthesis of aporphinoids.\(^9\)

\[
\begin{align*}
\text{R}^1 & \xrightarrow{\text{HCl (1.3 equiv), (COCl)}_2 \text{AcOEt}} \text{R}^1\text{R}^2\text{R}^3\text{R}^4\text{R}^5\text{NO} & \xrightarrow{\Delta (130-140 \degree \text{C}), 2-3 \text{ h}} \text{R}^1\text{R}^2\text{R}^3\text{R}^4\text{R}^5\text{CONH} \\
\text{R}^1 = \text{R}^2 = \text{R}^4 = \text{R}^5 = \text{H}, & \text{R}^1 = \text{OMe}, \text{R}^2 = \text{R}^4 = \text{R}^5 = \text{H} (85\%)
\end{align*}
\]

(F) Czifrák et al. reported a dehydration of per-O-benzoylated C-(1-azido-1-deoxy-α-D-glucopyranosyl)formamide by oxalyl chloride/DMF to give the corresponding nitrile in moderate yields.\(^10\)

\[
\begin{align*}
\text{R}^1\text{O} & \xrightarrow{\text{(COCl)}_2, \text{DMF}} \text{R}^1\text{R}^2\text{R}^3\text{R}^4\text{R}^5\text{CON} & \text{R}^1 = \text{R}^3 = \text{R}^4 = \text{R}^5 = \text{H}, \text{R}^2 = \text{OMe}, \text{R} = \text{Me} (96\%) \\
\text{R}^1 = \text{R}^3 = \text{R}^4 = \text{R}^5 = \text{H}, \text{R}^2 = \text{OMe}, \text{R} = \text{Me} (65\%) \\
\text{R}^1 = \text{R}^2 = \text{OMe}, \text{R}^4 = \text{R}^5 = \text{H}, \text{R} = \text{Me} (39\%) \\
\text{R}^1 = \text{R}^2 = \text{R}^3 = \text{H}, \text{R}^4 = \text{OMe}, \text{R} = \text{p-MeOPh} (61\%)
\end{align*}
\]

(G) Ehsan and Langer reported the use of oxalyl chloride in the synthesis of functionalized 3-hydroxymaleic anhydrides by cyclization of 1,1-bis(trimethylsilyloxy)ketene acetals.\(^11\)

\[
\begin{align*}
\text{R}^1\text{O} & \xrightarrow{\text{MeSiOTf (0.5 equiv), (COCl)}_2} \text{R}^1\text{R}^2\text{R}^3\text{R}^4\text{R}^5\text{CON} & \text{R} = \text{Ph} (70\%) \\
& \text{R} = 4-\text{MeC}_6\text{H}_4 (73\%) \\
& \text{R} = 3,4-(\text{MeO})_2\text{C}_6\text{H}_3 (70\%)
\end{align*}
\]

References


