

## Simple Transformation of Nitrile into Ester by the Use of Chlorotrimethylsilane

Fen-Tair Luo\* and Arumugasamy Jeevanandam

Institute of Chemistry, Academia Sinica, Nankang, Taipei, Taiwan 11529, Republic of China

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**Abstract:** Treatment of nitriles with alcohol and chlorotrimethylsilane at 50°C for 4 h could give esters in fair to good yields. Under similar reaction conditions, intramolecular lactonization *via* the concomitant nitrile and hydroxy groups in good yield were also demonstrated. © 1998 Elsevier Science Ltd. All rights reserved.

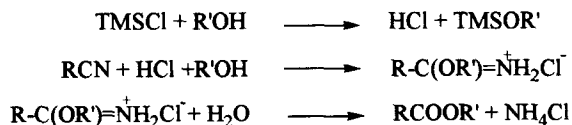
**Keywords:** Esterification, Lactonization, Nitriles, Esters, Chlorotrimethylsilane.

The use of hydrogen halide generated *in situ* from TMSX and water is an important reaction especially when HX is needed in requisite amount and under dry reaction conditions.<sup>1</sup> As part of our endeavor to utilize HX thus generated,<sup>2</sup> we have found TMSCl and alcohol can be used for the transformation of nitriles into esters with satisfactory yields. Since the conversion of nitriles into esters are potentially useful in organic synthesis.<sup>3</sup> There are several reports in the literature to bring about the same transformation, however, a new approach is still needed. In addition, most of the procedures reported in the literature to the preparation of esters from nitriles involves using either gaseous HCl or strong acid at higher temperature.<sup>4</sup> Furthermore, the preparation of sterically hindered ester was only obtained in low yield (ca. 20%) when HCl, isopropanol and nitrile were used.<sup>5</sup> Herein, we reported the scope of the transformation from various nitriles into esters or lactones by the use of alcohols or the concomitant hydroxyl group in the same molecule.

As a typical procedure, EtOH (0.75 mL, 13.38 mmol), TMSCl (0.68 g, 6.23 mmol), and *p*-nitrobenzyl nitrile (0.50 g, 3.08 mmol) were sequentially added to a dry flask under a nitrogen atmosphere at room temperature. The reaction mixture was heated at 50°C for 4 h. After being cooled to the room temperature, water (0.12 mL, 6.66 mmol) was added to the mixture and followed by the addition of Na<sub>2</sub>CO<sub>3</sub> (0.33 g, 3.11 mmol) and CH<sub>2</sub>Cl<sub>2</sub> (10 mL). After drying over MgSO<sub>4</sub> and concentration at low pressure could afford esters in 92% yield and with GC purities ≥ 98% as shown in **Table I**.

Solvent is not needed in this transformation except the case of intramolecular cyclization to form the lactone ring (Entries 9 and 10). Attempts to use THF, CH<sub>2</sub>Cl<sub>2</sub> or toluene in intermolecular esterification result in poor yields, even prolonging the reaction time. No ortho-esters were found in this reaction as detected by <sup>1</sup>H-NMR and GC/MS analysis even using alcohol as the solvent in running the reaction. In the case of using isopropanol, we found that adding 1 equiv of water prior to the addition of this more hindered alcohol could give better yields (Entries 11 to 14). Using more hindered alcohol such as *t*-butanol, we only obtained the corresponding *N-t*-butylamide in 70 to 80% yields as the isolated product. Protonation of the nitrile by HCl, generated *in situ* from TMSCl and the first equiv of alcohol or water, followed by nucleophilic attack of another equiv of alcohol and the hydrolysis of the iminium salt seemed to be the plausible pathway for this reaction (**Scheme I**).

### Scheme I. Plausible Reaction Pathway for the Ester Formation from Nitrile





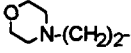



The intramolecular cyclization of hydroxy group with nitrile group to give benzofuranones is noteworthy. Thus, 3-hydroisobenzofuran-1-one (phthalide) can be formed from 2-(hydroxymethyl)benzenecarbonitrile with ethylene dichloride as the solvent (Entry 9). 3-Hydrobenzo[b]furan-2-one (2-coumaranone) can be formed by treating 2-(2-hydroxyphenyl)ethanenitrile with TMSCl first and followed by heating with *p*-toluenesulfonic acid (1 equiv) under reflux for 3 h in ethylene dichloride (Entry 10).

Since we used only 2 equiv amount of water in the usual work up procedure to form the esters, this method might be feasibly applied to the other moisture sensitive compounds. Further studies of using various nucleophiles to attack the nitrile group are still under investigation.

**Table I.** Transformation of Nitriles into Esters by the Use of TMSCl and Alcohols.

$$\text{R-CN} + \text{TMSCl} + 2 \text{ EtOH} \longrightarrow \left[ \text{R-C(OEt)=}\overset{+}{\text{N}}\text{H}_2\text{Cl}^- \right] \xrightarrow{\text{H}_2\text{O}} \text{RCOOEt}$$

Entry	Nitrile R=	Yields	Entry	Nitrile R=	Yields
1	Ph-	86%			
2	<i>p</i> -NO <sub>2</sub> -PhCH <sub>2</sub> -	92%	9 <sup>c</sup>		68%
3 <sup>a</sup>		71%	10 <sup>d</sup>		74%
4	EtOOC-CH <sub>2</sub> -	86%	11		73%
5 <sup>a</sup>	 N-(CH <sub>2</sub> ) <sub>2</sub> -	75%	12 <sup>e</sup>		69%
6	PhCH <sub>2</sub> -	93%	13 <sup>e</sup>	Ph-	71%
7	-(CH <sub>2</sub> ) <sub>4</sub> -	70%	14 <sup>e</sup>	Ph-CH <sub>2</sub> -	73%

<sup>a</sup> In addition to the amount of reagent used in the typical procedure, one more equiv of TMSCl and EtOH were used. <sup>b</sup> MeOH was used to afford the corresponding methyl ester. <sup>c</sup> The product was phthalide. <sup>d</sup> The product was 2-coumaranone. <sup>e</sup> Isopropanol and water were used to form the isopropyl esters.

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