

## NON-HYDROLYTIC CLEAVAGE OF ESTERS WITH MAGNESIUM IODIDE IN APROTIC NON-POLAR SOLVENTS

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*Summary* An efficacious procedure for the hydrolysis of primary, secondary and tertiary carboxylic esters with magnesium iodide in aprotic non-polar solvents, carbon disulphide and toluene, is reported

The hydrolysis of esters to the corresponding carboxylic acids is classically accomplished by acidic or basic hydrolysis in protic medium. This procedure has the disadvantage of the potential occurrence of side reactions, particularly when complex multifunctional molecules are involved.<sup>1</sup> Moreover, sterically hindered esters can be hydrolyzed only under strong reaction conditions. This prompts us to report on a novel non-hydrolytic procedure for the cleavage of esters.

The earliest methods of this type reported were based on the reaction of esters with lithium iodide in pyridine or 2,6-lutidine under reflux conditions.<sup>1,2</sup> Practical application of this method is limited only to methyl esters, while ethyl esters demanded rather drastic conditions.<sup>1</sup> The cleavage of primary esters (methyl, ethyl and benzyl) can also be accomplished by heating a solution of the ester with trimethylsilyl iodide at 100°C,<sup>3</sup> or with aluminium triiodide.<sup>4</sup> When this reaction was used to cleave tertiary esters, the yield was considerably lower (50%)<sup>5</sup> than that obtained from esters of branched acids.<sup>3</sup>

During our earlier work, we found anhydrous magnesium iodide to be an effective electrophilic reagent for the cleavage of C-O bonds in substrates such as vinyl triflates,<sup>6</sup> *gem*-bistriflates<sup>7</sup> and allyl<sup>8</sup> and tertiary alcohols<sup>9</sup> provided a non-polar, aprotic solvent such as toluene, benzene or carbon disulphide, which have little (CS<sub>2</sub>) or no tendency (toluene or benzene) to be coordinated to the magnesium ion, was used. The reaction products obtained in good yields were the corresponding iodo derivatives resulting in the formation of a C-I bond.<sup>9</sup>

Herein we report the use of magnesium iodide for the cleavage of C-O bonds in aromatic and aliphatic carboxylic esters **1**. The reaction conditions and results obtained are summarized in Table 1.<sup>10</sup>

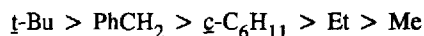
**Table 1** Results obtained in the reaction between esters and magnesium iodide in non-polar solvents

Substrate R-COOR'	R		Solvent	T (°C)	Time (days)	Yield <sup>a</sup> (%)
	R	R'				
<b>1a</b>	<i>n</i> -C <sub>11</sub> H <sub>23</sub>	Me	CS <sub>2</sub>	46	3	n r
			toluene	111	3	45
<b>1b</b>	<i>n</i> -C <sub>11</sub> H <sub>23</sub>	<i>c</i> -C <sub>6</sub> H <sub>11</sub>	CS <sub>2</sub>	46	5	n r
<b>1c</b>	<i>n</i> -C <sub>11</sub> H <sub>23</sub>	PhCH <sub>2</sub>	toluene	111	2	70
<b>1d</b>	<i>n</i> -C <sub>11</sub> H <sub>23</sub>	<i>t</i> -Bu	CS <sub>2</sub>	46	1.5	62
			toluene	111	1	80
<b>1e</b>	3-Me-C <sub>6</sub> H <sub>4</sub>	Me	toluene	111	3	48
<b>1f</b>	3-Me-C <sub>6</sub> H <sub>4</sub>	<i>c</i> -C <sub>6</sub> H <sub>11</sub>	toluene	111	2	78
<b>1g</b>	3-Me-C <sub>6</sub> H <sub>4</sub>	PhCH <sub>2</sub>	CS <sub>2</sub>	46	5	5
			toluene	111	1	67
<b>1h</b>	3-Me-C <sub>6</sub> H <sub>4</sub>	<i>t</i> -Bu	CS <sub>2</sub>	46	1.5	65
			toluene	111	1	80
<b>1i</b>	<i>t</i> -Bu	Me	toluene	111	3	48
<b>1j</b>	3-Me-C <sub>6</sub> H <sub>4</sub>	Et	toluene	111	3.5	41
<b>1k</b>	Me	1-adamantyl	CS <sub>2</sub>	46	1	95 <sup>b</sup>
<b>1l</b>	Me	2-adamantyl	CS <sub>2</sub>	46	3	96 <sup>b</sup>

<sup>a</sup> Yield of the isolated products, n r = no reaction. All products showed spectroscopic data consistent with those reported in the literature.

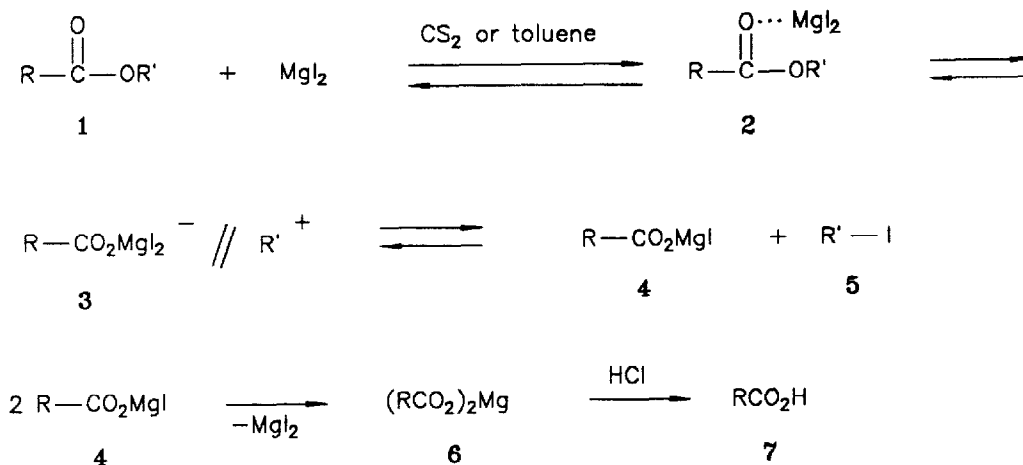
<sup>b</sup> Yield of the corresponding alkyl iodide **5**.

While no exact measurements of the reaction kinetics were made, the time required for completion of the reaction (Table 1) shows the reaction rate to be quite independent of the nature (aromatic or aliphatic) and steric hindrance of the acyl rest R of the ester. Thus, methyl pivalate **1i** reacted in toluene at a rate comparable to those of the other methyl esters **1a** and **1e** studied. As far as the alkyl rest R' is concerned, the following sequence of reactivity can be drawn



The reaction is chemoselective as seen by the fact that either primary and secondary esters do not react or require longer reaction times giving only poor yield of the carboxylic acids when carbon disulphide was used as the solvent (Table 1). However, in toluene all the esters are cleaved to give the acids **7** in moderate to good yields.

The data obtained suggest that the slow step of the process involves the ionization of a complex **2** formed by coordination of the ester **1** to one (or more) molecule(s) of magnesium iodide to yield the ion-pair **3**, from which the salt **4** and the alkyl iodide **5** are formed, Scheme 1. The decomposition of **4** yields the magnesium salt **6**, which precipitates in the non-polar solvents used, thereby - perhaps - contributing to the displacement of equilibrium towards the final reaction products **5** and **6**.



Scheme 1

Although we did not attempt to isolate the alkyl iodides **5** obtained from **1a-j** as by-products, the reaction between an ester and magnesium iodide can also be regarded as a convenient procedure for replacement of an acyloxy group with an iodide atom. With this aim in mind, we obtained the corresponding iodides **5k** and **5l** from 1- and 2-adamantyl acetates **1k** and **1l**, respectively, by reacting with magnesium iodide in carbon disulphide.

In summary, we have found a mild method to hydrolyze carboxylic esters under non-hydrolytic conditions. Our method allows also the cleavage of sterically hindered esters under mild conditions. Further extension of our method to functionalized carboxylic esters are in progress.

### References

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- 10 General Procedure for the cleavage of esters **1**. To a suspension of anhydrous  $MgI_2$  (1.3 g, 5 mmol) in the appropriate solvent (15 ml, Table 1) was added a solution of the ester **1** (3 mmol) in the same solvent (5 ml). The mixture was refluxed under exclusion of moisture, cooled and poured into 10% aqueous  $NaHCO_3$  (100 ml). The alkyl iodide **5** obtained was isolated by extraction with  $CH_2Cl_2$  (3 x 20 ml), the combined organic layers were washed with 10% aqueous  $NaHSO_3$  (25 ml) dried and the solvent removed, 1- and 2-adamantyl iodides (**5k** and **5l**) were purified by column chromatography (silica gel/*n*-pentane) of the residue remained after the removal of solvent. The carboxylic acid was isolated by acidification of the aqueous phase with 15% HCl followed by extraction with  $Et_2O$  (3 x 20 ml). The combined organic layers were washed with water, dried over  $MgSO_4$  and the solvent removed. The acid obtained was purified by recrystallization.
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