Chlorotrimethylsilane, a suitable reagent for the esterification of diverse functionalized carboxilic acids

ERAS JOLI, JORDI*, VILARÓ JORDANA, FRANCISCA** and CANELA GARAYOA, RAMÓN*,**

* *Chemistry Department, Lleida University, 25198-Lleida, Spain.*
** *Centre UdL-IRTA, Lleida University, Rovira Roure, 191, 25198-Lleida, Spain.*

Resumen:

Una amplia variedad de ácidos carboxílicos funcionalizados se pueden convertir en sus correspondientes ésteres de alquilo con un alcohol y clorotrimetilsilano. La reacción no afecta los diferentes grupos funcionales distintos al grupo carboxilo en las condiciones de reacción ensayadas.

Abstract:

A wide variety of functionalized carboxylic acids can be converted into the corresponding alkyl esters upon treatment with alcohol and chlorotrimethylsilane. The reaction does not affect functional groups different from a carboxylic one in the tried conditions of reaction.

Key words: functionalized carboxylic acids, chlorotrimethylsilane, esterification

INTRODUCTION

Functionalized carboxylic acids are widely present in nature as acylglycerides, complex lipids or free acids. (1) Their presence has a significance as a taxonomic classification, with hormonal and metabolic functions and to evaluate the nutritional or toxic relevance of organisms. (2) The determination of the presence of these functionalized carboxylic acids is usually conduced by GLC or GLC-MS previous esterification to volatile esters. However, the majority of the procedures described produce artifacts as well as chemical decomposition and the subsequent loss of some of these acids. (3,4)

Chlorotrimethylsilane have been projected as a catalysis to esterify acids and transesterify esters. (5,9) Recently, chlorotrimethylsilane has been introduced as an acid catalyst reagent for GLC analysis of saturated and unsaturated fatty acids. (6) It allows complete derivatization of extracted fat of samples. It can also be applied

Correo electrónico: eras@quimica.udl.es - vilaro@quimica.udl.es - canela@quimica.udl.es

directly to the sample, named direct derivatization, with advantages over other well-established methods of derivatization. (7a,7b)

In order to advance on the possibility to extend the developed method to diverse functionalized carboxylic derivatives, a set of acids wearing diverse functional groups (**1**) were esterified using different alcohols (**2**) and chlorotrimethylsilane (figure 1).

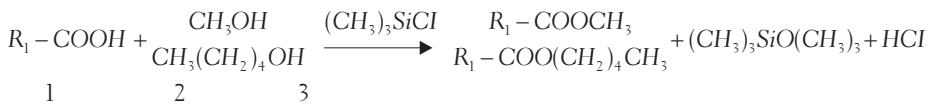


Figure 1

Commercial esters, when available, were used to follow the reactions and to determine the final yields.

METHODOLOGY

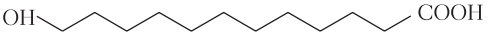
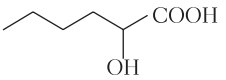
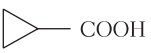
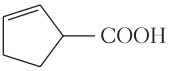
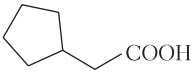
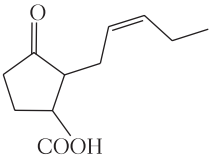
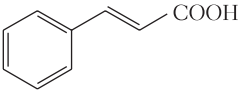
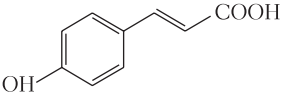
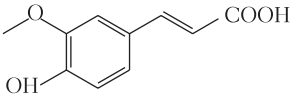
General Experimental Procedure: 1.5 mmol of 3-cyclopentylpropionic acid, 50 mmol of methanol and 3.5 mmol of chlorotrimethylsilane were added to a screw Teflon cap vial filled with nitrogen. The reaction mixture was heated and magnetically stirred at 60ºC for 2 h. After cooling, the mixture was diluted with diethyl ether and neutralized with saturated sodium bicarbonate solution. The organic solution was dried over anhydrous magnesium sulfate and evaporated to dryness with a nitrogen stream. The purity of the crude of the reaction was assessed by TLC, GLC and GLC-MS.

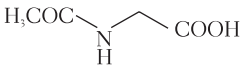
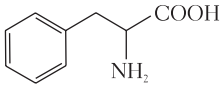
DISCUSSION AND RESULTS

As Table 1 shows, hydroxy, oxo and N-acetyl groups are stable in the tryed conditions. Carboxylic acids wearing present in? these groups are fully converted to the corresponding alkyl esters (**3**) without detecting the presence of any by—products. The yields corresponding to the isolated products are always higher than 80%.

Similar results were described by Gerspacher et ál (8) for the esterification of saccharic acid. The presence of double bounds, either isolated or conjugated with aromatic rings, does not seem to cause any problem either. These results are already in accordance with those that show that unsaturated fatty acids like oleic, linoleic and linolenic acids are fully stable under these conditions (9). The stability of cyclopropane rings is also remarkable. Thus, the cyclopropanecarboxylic acid was fully converted to the corresponding ester. In this case, the corresponding product was not isolated because of its high volatility. Chrysanthemic acid, a not so stable compound, was also transformed to the corresponding ester with 95% yield, although, in this case, the reaction was carried out at 25ºC to avoid the partial decomposition observed when the reaction was carried out at 60ºC.

Table 1. Esterification of functionalized carboxylic acids

Carboxylic acid	% Conversion[a]	% Yield[b]
12-hydroxidodecanoic acid 	100	91
2-hydroxyhexanoic acid 	100	84
Cyclopropanecarboxylic acid 	100	-[c]
2-cyclopenten-1-acetic acid 	100	71
3-cyclopentilpropionic acid 	100	83
(±)-1α,2β-3-oxo-2-(*cis*-2-pentenil)-cyclopentaneacetic acid (jasmonic) 	100	82
2,2-dimethyl-3-(2-methyl-1-propenil) cyclopropanecarboxylic acid (chrisantemic) 	96[d]	95
3-phenyl-2-propenoic acid (cinnamic) 	100	86
3-(4-hydroxi)phenyl-2-propenoic acid (coumaric) 	100	71
3-(4-hydroxi-3-metoxi)phenyl-2-propenoic acid (ferulic) 	98	96

Carboxylic acid		% Conversion[a]	% Yield[b]
N-acetylglicine		100	81
L-phenylalanine		100	85

[a] as methyl and pentyl ester.
[b] as methylester.
[c] as propylester.
[d] the ester was not isolated.
[e] (+)-*t*-chrysanthemic acid, the esterification was carried out at room temperature for 6 h.

The method can be applied to free amino acids. In this case, the treatment with sodium bicarbonate of the crude of reaction allows recovering the alkyl aminoester as a free base. Although Brook and Chan already described the esterification of amino acids using chlorotrimethylsilane, they did not either use the acetyl group as a protecting group. They did not recovered the esterified aminoacid as a free base.[5]

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