Dibutyltin oxide mediated synthesis of esters assisted by microwave irradiation

Julio A. Seijas[a,*] Carolina Mendez-Gálvez[b], M. Pilar Vázquez-Tato[a*]

[a]Dpto. Química Orgánica. Facultad de Ciencias, Universidad de Santiago de Compostela. Campus Lugo. Aptdo. 280. 27080-Lugo. Spain.
[b]Facultad de Ciencias. Universidad de Chile. Santiago de Chile. Chile
julioa.seijas@usc.es; pilar.vazquez.tato@usc.es

Abstract

The use of dibutyltin(IV) oxide in microwave assisted synthesis of esters from alcohols and acids under solvent free conditions (MASFOS) in high yields is described.

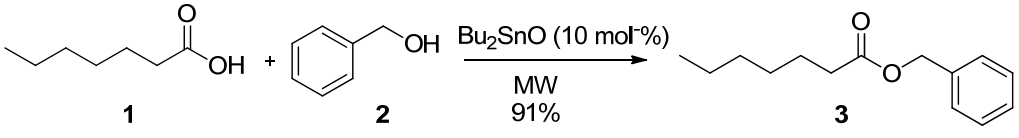
Introduction

Syntheses of esters from carboxylic acids and alcohols include a large number of alternatives, always in the presence of a catalyst.[1] Tin alkoxides, especially organotin(IV) alkoxides, are extremely useful because the tin-oxygen bond is readily formed, thanks to its thermodynamic stability, while this bond is reactive enough to attack electrophiles. This is used mainly in carbohydrate chemistry, however, carboxylic acid derivatives (chlorides or anhydrides) are employed frequently instead of the free acids.

On the other hand, the experience of our group in MAOS (microwave assisted organic synthesis)[2] has proven in several times that this methodology is a valuable tool in enhancing organic reactions, with the possibility of working in many cases in the absence of solvent. The examples in the literature about the use of microwave irradiation in esterifications catalyzed by Bu_2SnO were performed with acid chlorides,[3] however some examples on the lactonization hydroxyacids under conventional conditions[4] led us to revise the possibility of achieving conditions for esterification of carboxylic acids and alcohols.

Results

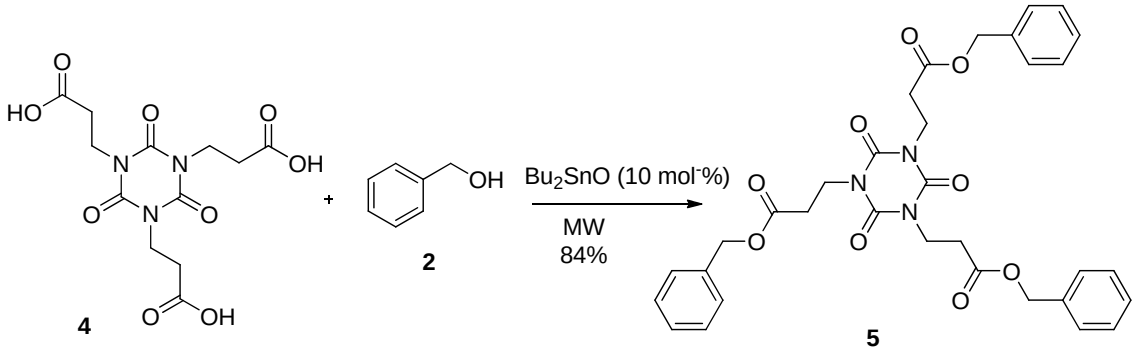
As reaction model, esterification of heptanoic acid and benzyl alcohol was studied (Scheme 1). So, an equimolecular mixture of both components in the presence of a catalytic ammount of Bu_2SnO (10 mol-%), was irradiated in a monomode microwave oven (CEM Discovery) at 180ºC. The reaction was carried out in an open vessel and monitored by thin layer chromatography, being completed after 50 minutes. At higher temperatures different degrees of carbonization were observed, meanwhile lower temperatures lead to longer reaction times. The yield of benzyl heptanoate after additional column chromatography purification was 91%.



1 **2** **3**

Scheme 1.

The potential of the reaction was established when we applied this methodology to the to the synthesis of tripodal esters like 3-{3,5-bis[3-(benzyloxy)-3-oxopropyl]-2,4,6-trioxo-1,3,5-triazinan-1-yl}propanoate (**5**), which are potential candidates to be used as cores in the synthesis of dendrimers. So, under the same reaction conditions, 84% yield of triester **5** was obtained after column chromatography purification (Scheme 2).



Scheme 2.

In summary, the direct conversion of alcohols and acids under MASFOS (microwave asisted solvent free organic synthesis) is presented. The procedure is applicable with carboxylic acids mono- and polyfunctionalized.

General experimental procedure

A mixture of benzyl alcohol (0.16 g, 1.5 mmol) and 3-[3,5-bis(2-carboxyethyl)-2,4,6-trioxo-1,3,5-triazinan-1-yl]propanoic acid (**4**) (0.14 g, 0.5 mmol) were irradiated with microwaves (300 W power) in an open tube with stirring for 50 min at 180 °C, in the presence of dibutyltin(IV) oxide (10 mol-%). The crude was further purified by flash column (silica gel, EtOAc:Hex, 1:9) obtaining ester **5** in 84% yield.

^{1}H NMR (300 MHz, $CDCl_3$) δ 2.70 (6H, dt, J=7 Hz, J=3 Hz) 4.15 (6H, br t, J=7 Hz) 5.11 (br s, 6H), 7.29-7.77 (m, 15H).

Acknowledgements

XUNTA DE GALICIA for financial support: INCITE09 262346PR. Comisión Nacional de Investigación Ccientifica y Tecnológica" (CONICYT) Chile, for a fellowship to CMG

Literature

(1) Otera, J. *Esterification. Methods, Reactions, and Applications*; Wiley-VCH: Weinheim, 2003.
(2) Seijas, J. A.; Vazquez-Tato, M. P.; Crecente-Campo, J. *Tetrahedron* **2010**, *66*, 8210.
(3) Morcuende, A.; Ors, M.; Valverde, S.; Herradon, B. *J. Org. Chem.* **1996**, *61*, 5264.
(4) Steliou, K.; Poupart, M. A. *J. Am. Chem. Soc.* **1983**, *105*, 7130.