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Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry

Publication details, including instructions for authors and subscription information: http://www.tandfonline.com/loi/lsyc20

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To cite this article: André Loupy, Philippe Pigeon, Mohamed Ramdani & Patrick Jacquault (1994): Solid-Liquid Phase Transfer Catalysis Without Solvent Coupled with Microwave Irradiation: A Quick and Efficient Method for Saponification of Esters, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 24:2, 159-165

To link to this article: http://dx.doi.org/10.1080/00397919408013814

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SYNTHETIC COMMUNICATIONS, 24(2), 159-165 (1994)

SOLID-LIQUID PHASE TRANSFER CATALYSIS WITHOUT SOLVENT COUPLED WITH MICROWAVE IRRADIATION: A QUICK AND EFFICIENT METHOD FOR SAPONIFICATION OF ESTERS

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Abstract: Hindered esters can be easily saponified in a few minutes using microwave activation under solid-liquid PTC conditions without solvent. A monomode microwave reactor (Maxidigest MX 350 Prolabo) is the most efficient. A non thermal effect of microwaves is evidenced by reference to classical heating.

Some years ago, we showed that solid-liquid phase transfer catalysis (PTC) without solvent is an efficient method to saponify hindered esters¹. When applied to mesitoic esters, a system consisting of 5 mol. equiv. of powdered KOH (as a commercial base containing about 15 % water) and 10 % Aliquat 336 was shown

to be by far the most efficient system to promote the reaction. This method constituted a considerable enhancement in experimental conditions and yields when one considers the proposed solutions including cryptates², "anhydrous hydroxide" ³ or triphase catalysis ⁴.

However, some further improvements were necessary due to rather long reaction times: 5 hours at 85 °C with methyl mesitoate (yield = 93 %) or octyl mesitoate (yield = 87 %). For this reason, use of microwave activation to reduce harshness of experimental conditions was attempted. It was claimed that this method could induce very quick and efficient reactions. It was the case especially in the absence of solvent, either using supported reagents onto mineral oxides ⁵ or PTC conditions ^{6,7}. Two kinds of microwave reactors were used in this study:

i) a domestic oven (multimode system) Philips Whirlpool AT 5964,

ii) a focused microwave digester ⁸ (monomode system) Prolabo Maxidigest MW 350

A variety of esters was investigated including benzoic esters 1 and 2, hindered ones as mesitoates 3 and 4, long chains substrates 5 and a menthyl ester 6, widely used in asymmetric synthesis.(scheme 1)

The previous experiments were performed in the domestic multimode oven using a system consisting of 2 mol. equiv. of KOH and 0.1 eq. Aliquat 336 as saponyfing agent for methyl and octyl benzoates or mesitoates (Table I). Scheme 1

 $\begin{array}{c} O \\ R-C-O-R' \\ \hline 2) HCl \end{array} \qquad \begin{array}{c} O \\ R-C-O-H \\ \hline \end{array}$

1
$$R = Ph$$
 $R' = Me$ 2 $R = Ph$ $R' = n C_8H_{17}$
3 $R = \bigcirc$ $R' = Me$ 4 $R = \bigcirc$ $R' = n C_8H_{17}$

5 $R = nC_{17}H_{35}$ $R' = nC_8H_{17}$ 6 R = Ph R' = d-menthyl

-TABLE I-

Saponification of esters using 2 eq. KOH-0,1 eq-Aliquat							
in a domestic microwave oven (Power = 250 W)							
Ester	Irradiation Time	Yield (%)					
1	30 sec.	87					
2	1 min.	83					
3	2 min.	75					
4	2 min.	57					

If yields are rather satisfactory with benzoic esters, they are less interesting with mesitoic esters.

In order to improve yields, the monomode reactor was used. Effects of incident power as well as those of base amounts were checked with all the abovementioned esters (Table II).

Saponification with the Maxidigest MX 350 digester system									
Ester	KOH mol. equiv.	Microwave		Yield	Final ^{a)}				
		Power(W)	time (min)	%	Temperature °C				
1	2 or 5	30	7	94					
	2	90	1	96	205				
2	2 or 5	30	5	92					
	2	90	2	94	210				
3	5	30	8	88					
	2	90	2	87	240				
4	5	30	10	85					
	2	90	4	82	223				
5	5	30	6	73					
	2	90	5	79	145				
6	2	120	4	87	218				

-TABLE II-

a) Evaluated by a luxtron optical fibre thermometer or by introducing a digital sensing probe at the end of irradiation.

Excellent yields in expeditive conditions are obtained. They are comparable or even better to those described under classical heating for longer time ¹⁻⁴. We have also to point out that, contrary to the observation under conventional heating, 2 molar equivalents of KOH are now sufficient (instead of 5 equivalents). When compared to results obtained with multimode domestic oven, those achieved from the monomode system are clearly better (e.g. 4 : 82 % versus 57 %). This conclusion underlines once more the special efficacy of this system 7,9,10.

Finally, a non thermal effect of microwave activation, eventually due to entropic or "hot spots" effects has to be questioned¹¹. To this purpose, experiments were performed in an oil or a sand bath at the same temperature and for the same time as for microwave irradiation. (Table III)

			Yi	Yield of acid	
ester %		conventio	microwave		
			acid %	starting ester %	%
1	1 min	205°C	90	-	96
2	2 min	210°C	72	-	94
3	2 min	240°C	38	45	87
4	4 min	223°C	0	100	82
5	5 min	145°C	77	-	79
6	4 min	218°C	66	14	87

-TABLE III-

From this table, it can be clearly seen that microwave activation presents significant advantages when compared to conventional heating. Not only are the yields better, *indicative of a specific effect of microwave*, but also experiments are considerably easier to perform with a very simplified work-up.

Moreover it would seems that the non specific thermal effect of microwaves is more important when reactions are more difficult classically: e.g. methyl benzoate 96 % versus, 90 % in conventional heating (oil bath), with methylmesitoate 87 % versus 38 %, and especially with octyl mesitoate 82% versus 0%.

In conclusion, a new efficient procedure of saponification is described. It involves KOH-Aliquat in the absence of organic solvent and microwave activation using a focused open-vessel digestion system. Microwave irradiation appears to be largely more efficient than classical heating under identical conditions of time and temperature in very easy to perform experiments. Finally a non-thermal effect of microwave irradiation is evidenced essentially with poorly reactive esters.

Experimental

A mixture of the ester (25 mmol.), 10 % of Aliquat 336 (1 g; 2.5 mmol) and 2 eq. of KOH (3.25 g; 50 mmol.) were introduced into a pyrex tube which was then placed in a Maxidigest MX350 Prolabo microwave reactor fitted with a rotational system. Microwave irradiation was carried out for the times and at the power indicated (see Table 2). The mixture was cooled to ambient temperature and eluted with CH_2Cl_2 to remove the remaining ester and formed alcohol. The potassium salt of the acid is hydrolyzed with diluted HCl. After filtration and washing with water, the resultant acid was dried under vacuum. The acids were characterized by ¹H NMR and melting points by comparison with authentic samples.

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(Received in the UK 25 June 1993)