

## MICROWAVE ACTIVATED ACETYLATION OF SECONDARY ALCOHOLS WITHOUT SOLVENT AND SOLID SUPPORT

N. KAMMOUN, Y. LE BIGOT \*

*\* École Nationale Supérieure de Chimie de Toulouse  
Laboratoire de Catalyse, Chimie Fine et Polymères  
118, route de Narbonne - 31077 TOULOUSE Cedex 4 (France)*

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**RESUME:** L'acétylation de divers alcools a été réalisée sous micro-ondes en absence de solvant et de support solide. Si les alcools tertiaires n'ont pas conduit aux esters attendus, en revanche l'estérification d'alcools secondaires a été réalisée avec d'excellents rendements.

**ABSTRACT:** Acetylation of various alcohols was realised with microwave activation in the absence of solvent and solid support. Tertiary alcohols did not yield the expected esters but the acetylation of secondary alcohols was accomplished with excellent yields.

**KEY WORDS:** Esterification, secondary alcohol, acetic anhydride, microwave.

We have recently described a new route to esters which involves the reaction, without solvent and without catalyst, of secondary and tertiary alcohols with various reactive anhydrides [1]. Thermal activation is then required in order to achieve a proper evolution of the reaction.

The undeniable interest in such simplified reaction conditions led us to investigate the possibility of using microwave power to reach the transition state required for esters synthesis.

Indeed, microwaves have been used successfully to activate various organic synthesis reactions [2-6].

Widespread use of this technique is limited, however, because pressure bursts due to excessive rapid evaporation of volatile solvents or reactants may lead to explosions [3,7]. Microwaves have been used in heterogeneous media also. Such a set-up requires a selection of appropriate solid absorbent supports [8-13] or of specific phase transfer catalysts [13-15]. In any case, the extraction and purification of the final products are made more difficult.

Microwaves (electromagnetic radiation at 2,45 GHz) interact with matter to produce heat

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\* To whom correspondence should be addressed

according to an original process with the following characteristics: heat is generated homogeneously throughout the entire mass, avoiding superficial overheating. Contrary to classical heating which produces an inward heat gradient, microwave heating produces an even temperature rise. Microwaves act rapidly (up to 10°C/sec) by transferring electromagnetic energy to polar bonds in molecules. Friction due to increased agitation of molecules translates into heat.

We therefore sought to use microwaves, in the absence of solvents and of solid (absorbent supports or catalysts), for the synthesis of esters. Alcohol and acetic anhydride were mixed alone in the reactor in stoichiometric ratios.

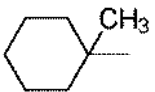
Our results show that acetylation of tertiary alcohols does not proceed with microwave activation, even in the case of 1-methylcyclohexanol which presents a relatively high boiling point (table I). Acetylation of this type of compound is better achieved by classical heating means (table I).

We suggest that the lack of microwave activation on the acetylation of tertiary alcohols is related to steric effects which are responsible for the inherent inertness of such alcohols.

However, the use of microwaves is shown to be very efficient in these same conditions in the acetylation of secondary alcohols, even under mild conditions such as weak power and brief activation periods (table II). Furthermore, the yield in ester can become practically quantitative if an excess of alcohol is used with respect to the stoichiometric amount (see b and c in table II). It is also noteworthy that the percentage of ester formation is directly related to the boiling point of the starting alcohol.

**Table I:** Acetylation of tertiary alcohols



R	Alc BP(°C)	Microwave activation			Classical heating		
		P (watts)	Time (mn)	Yield (%)	Tbath (°C)	Time (h)	Yield (%)
(CH <sub>3</sub> ) <sub>3</sub> C—	82	90	1	<2	105	7	39
	168*	120	1	<2	145	8	83

\* P = 752 mm Hg

**Microwave activation:** anhydride = alcohol = 5x10<sup>-2</sup> mole

**Classical heating:** anhydride = alcohol = 2x10<sup>-1</sup> mole

## EXPERIMENTAL PART

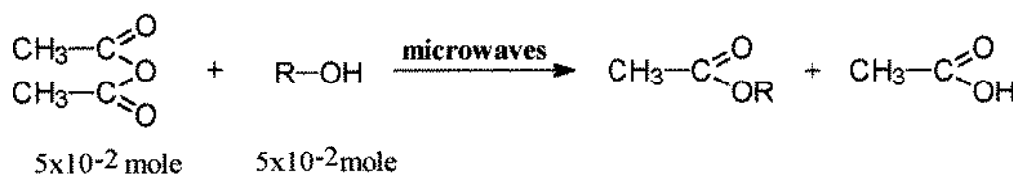
All the chemicals used are standard commercial products without prior purification.

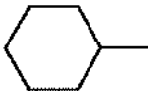
Reactions under microwaves were realised in a Prolabo Maxidigest 350 microwave oven at 2.45 GHz in a tubular Pyrex reactor equipped with a condenser. During irradiation, the reactor is subjected to oscillating rotations.

An alcohol-anhydride mixture in stoichiometric ratio is introduced in the reactor. It is then irradiated with the powers and during the times indicated in tables I and II.

Isopropyl acetate is purified according to the procedure described previously [1]. Cyclohexyl and 1-methyl cyclohexyl acetates are purified by chromatography on a silica gel column using a hexane/ether mixture (95/5) as eluting solvent.

**Table II:** Microwave acetylation of secondary alcohols



R (BP alc. °C)	P (Watts)	Time (mn)	$\Delta t^a$ (mn)	Yield (%)
 (167°C)	90	1	-	80
	105		-	85
	120		-	86
	150		-	86 (96 <sup>b</sup> )
	180		-	86 (99 <sup>c</sup> )
$(\text{CH}_3)_2\text{CH}-$ (82°C)	30	3x1	1	27.5
	45	3x1	1	37
	60	3x1	2	44
	75	3x1	4	58
	90	1	-	33

**a:**  $\Delta t$  = delay between two successive irradiations.

**b:** anhydride =  $5 \times 10^{-2}$  mole, alcohol =  $2 \times 5 \times 10^{-2}$  mole

**c:** anhydride =  $5 \times 10^{-2}$  mole, alcohol =  $3 \times 5 \times 10^{-2}$  mole

The  $^1\text{H}$  NMR spectra recorded in deuterated DMSO and elementary analyses of these compounds gave the following characteristics:

- Cyclohexyl acetate:

$\delta$  1.98 ppm (s, 3H,  $\text{CH}_3$ ) 4.63 ppm (m, 1H, CH)  
1.66-1.78 and 1.29-1.37 ppm (2m, 10H, cyclohexyl protons)

*Anal.* Found (calcd).  $\text{C}_8\text{H}_{14}\text{O}_2$ : %C 67.68 (67.60), %H 10.28 (9.85).

- 1-methyl, cyclohexyl acetate:

$\delta$  1.41 ppm (s, 3H,  $\text{CH}_3$ ) 1.95 ppm (s, 3H,  $\text{CH}_3$ )  
1.42-1.48 ppm (m, 10H, cyclohexyl protons).

*Anal.* Found (calcd).  $\text{C}_9\text{H}_{16}\text{O}_2$ : %C 69.32 (69.20), %H 10.70 (10.25).

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The reactions with microwaves were carried out in the Fundamental and Applied Heterochemistry Laboratory of Professor Jaques Dubac at the Paul Sabatier University of Toulouse. The authors wish to acknowledge his help. Thanks are also due to Christian Laporte of the same laboratory for practical advice in the use of the microwave oven.

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