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Synthesis of Long Chain Aromatic Esters in a Solvent-Free Procedure Under Microwaves

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Abstract: Alkylation with n-octyl bromide of several substituted benzoic acids was performed under solvent-free phase transfer catalysis with excellent yields (≥ 95 %) within very short times (2-7 min). Terephthalate octylation was raised from 20 % to 92 % under microwave activation when compared to conventional heating thanks to intrinsec effects of the radiation.

Key words: Microwaves / solid-liquid PTC without solvent / synthesis of long chain aromatic esters.

Introduction

In previous works, we have studied the alkylation under microwaves of potassium acetate by long chain halides. Quantitative yields were obtained within very short times (1-2 min.) either by performing the reaction in "dry media" conditions with impregnated reactants onto alumina[1,2] or under solvent-free solid-liquid Phase Transfer Catalysis (PTC)[3]. In a preliminar approach[4], the extension to potassium benzoate appeared to be rather limited with supported reagents onto alumina (47 %) whereas it seemed efficient under PTC conditions (99 % within 5 min.).

In the present work, we apply ourselves to the understanding of the involved phenomena and to the extrapolation of our first results to the synthesis of various substituted aromatic esters. In these cases, the reactivity of benzoate anions could be limited either by the acidity of ArCOOH or by the nucleophilicity of $ArCOO^-$. We also have to consider the possibility of reacting carboxylates prepared *in situ* from corresponding carboxylic acids and bases and, finally, to examine the most difficult case of dialkylation of terephthalic acid.

Results and Discussion

Thermal Behaviour of Potassium Benzoate under Microwaves

A preliminary study of thermal effects induced by the interactions microwaves-materials (potassium benzoate neat or in the presence of quaternary ammonium salts) was carried out to appreciate the changes in polarity of substrates.

Effectively, an increase in polarity results in a stronger adsorption of microwaves, and consequently to an increase in the raised temperature. We therefore (Figure) studied the thermal evolution during microwave expositions[5] of :

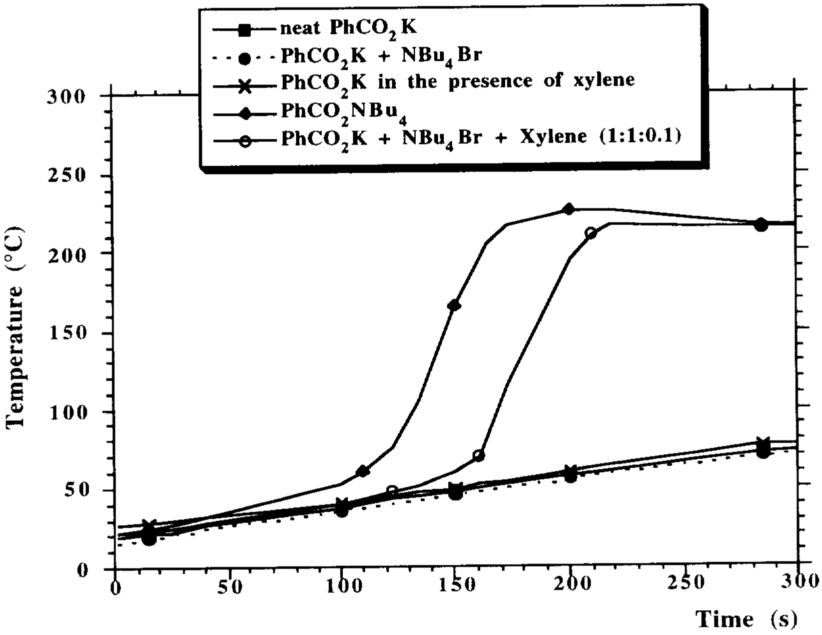


Figure : Thermal behaviour of Benzoates induced by microwaves under several conditions (mass of sample = 2g ; monomode microwave oven, 180 W)

The main conclusions we can draw from this figure are :

i) Firstly, $PhCO_2K$ behaves as a weak polar molecule (poorly dissociated) in connection with a tridimensionnal aggregation in the solid state (curves a and b).

ii) When one compare the behaviours of $PhCO_2NBu_4$ and of a 1:1 mixture $PhCO_2K$ + NBu_4Br (curves e and c), it is clear that there is no ion exchange in the solid state (no formation of $PhCO_2NBu_4$).

iii) The addition of small amount of xylene (which behaves only as an inert non-polar liquid phase) in the precedent solid mixture 1:1 provokes an important increase in temperature (curve d), indicative of the establishment of the ion exchange equilibrium after 3 minutes. The obtained curve is then comparable to that of $PhCO_2NBu_4$ (curve e) :

$$PhCO_2^- K^+ + NBu_4^+ Br^- \overset{+ \text{ liquid phase}}{\rightleftharpoons} PhCO_2^- NBu_4^+ + K^+ Br^-$$

This last observation is of prime importance as it gives an illustration of solid-liquid PTC mechanism. *There is necessity of a liquid organic phase to induce the ion-pair exchange.* This observation seems to be rather in favour of an interfacial mechanism for solid-liquid PTC[6]. In the case of a reaction, the alkylation agent (e.g., nOctBr) can play the role of organic poor-polar liquid (instead of unreactive xylene) and consequently can act both as electrophile and organic phase for the reaction[7].

Alkylation of Benzoic Acid

Two types of solvent-free PTC conditions were considered here :

„ Method A : Use of preformed potassium salt

$$\underset{10\ \text{mmoles}}{PhCO_2^-K^+} + \underset{10\ \text{mmoles}}{nC_8H_{17}Br} \xrightarrow[0.5\ \text{mmol}]{\text{Aliquat 336}} PhCO_2nC_8H_{17} + K^+Br^-$$

„ Method B : Generation *in situ* of the potassium salt from benzoic acid and a base and alkylation

$$\underset{1\ :\ 1\ :\ 1}{PhCO_2H + K^+B^- + n\,C_8H_{17}Br} \xrightarrow[5\%]{\text{Aliquat 336}} PhCO_2nC_8H_{17} + BH + K^+Br^-$$

The main results are given in Table I.

- Table I -

Synthesis of n-octyl benzoate by solid-liquid solvent free PTC

Method	Conditions		MW yield % a)	Δ yield % b)
A	2.5 min	150°C	99	99
B base = KOH	3 min	187°C	87	89
= K_2CO_3	**5 min**	**180°C**	**99**	**100**
= KOtBu	4 min	172°C	80	78

a) g c yield with internal standard under microwave irradiation (domestic oven 600 W)

b) g c yield under conventional heating in the same conditions.

It is obvious that methods A and B lead to comparable results and that **the previous preparation of the potassium salt is not necessary.**

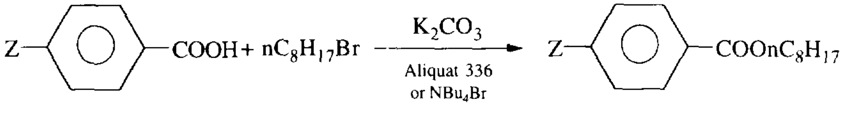
Results relative to base effects indicate that K_2CO_3, a weak non nucleophilic base, is the most adapted one [8]. The use of a stronger base is prejudicious certainly due to easy saponification of esters in these conditions when KOH is concerned[9] or to competitive etherification with KOtBu [10]:

$$Ph\,CO_2nC_8H_{17} + KOH \xrightarrow{\text{Aliquat 336}} PhCO_2^-K^+ + nC_8H_{17}OH$$

$$KOtBu + nC_8H_{17}Br \xrightarrow{\text{Aliquat 336}} nC_8H_{17}OtBu + K^+Br^-$$

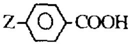
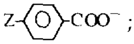
In all these experiments, it is clear that, every conditions equal elsewhere, microwaves behave as classical heating. In accordance with several publications[11-14], *microwave effect is here limited to pure thermal effects*. Especially, the acid-base equilibrium was shifted to the right by evaporation of light polar species (e.g. $H_2O \geq 100°C$).

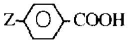
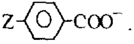
p-Substituted Aromatic Esters



$Z = NMe_2$, OMe, H, CN, NO_2

As the whole procedure can involve two steps, the electronic substituents effects can affect the reaction in two contradictory ways :

- electron-withdrawing groups lead to an increase in the acidity of  and consequently a shift to the right of acid-base equilibrium, but to a decrease in nucleophilicity of  ;

- reciprocally, electron-donating groups lead to a reduction in the acidity of  but to an increase in nucleophilicity of  .

In table II are indicated the results obtained under multimode microwave (600 W) by the two indicated methods involving preformed potassium salt from alcoholic solution of the corresponding acid and potassium hydroxide (A) or the carboxylate salt generated *in situ* (B).

-Table II -

Synthesis of p-substituted octyl benzoates by solid-liquid solvent free PTC.

Transfer agent = $NBu_4^+ Br^-$ (TBAB) [10 %] - Domestic microwave oven 600 W.

Z	Reaction time (min)	Method A		Method B , K_2CO_3	
		T °C [a)]	yield % [b)]	T °C [a)]	yield % [b)]
H	2.5	150	99	145	**99**
NMe_2	3	202	97	140	**100**
OMe	2	174	82	145	**98**
CN	3	-	80 [c)]	202	**95**
NO_2 [d)]	2	202	81	205	**95**

a) final temperature measured at the end of irradiation

b) g c yield using an internal standard

c) in closed Teflon vessel

d) Aliquat 336 as transfer agent instead of TBAB (A ⇒ 66 % ; B ⇒ 74 %)

It is obvious to state that **yields are nearly quantitative within 2-3 minutes whatever the substituent is.** In such conditions, the intrinsec effects of substituents disappear as masked by the high temperature level. **The superiority of Method B** is here evident as yields are even better than with method A. Furthermore, there is no need to prepare in an independent way the potassium salt previously to alkylation.

The experiments described here constitute a large improvement when compared to those of literature using solvents and which need rather long reaction times (8-24 h)[15,16] and previous salt preparation[15]. They consider biphasic systems including chlorobenzene or acetonitrile as solvents for the synthesis of the p-nitro compound.

In order to check the possibility of intervention of non-thermal effects of microwaves, we have performed several experiments in the same conditions (time, temperature) in a thermostated oil bath (Table III).

- Table III -

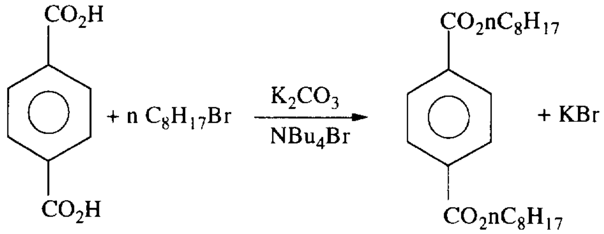
Comparison of octylation under conventional heating or microwave exposition (method B)

Z	Conditions		Yields %	
	T°C	t_{min}	oil bath	microwave
H	145	2.5	99	99
OMe	145	2	98	98
CN	202	2	95	95

The reduction in reaction times is here only the consequence of temperature level raised as **microwave revealed here only thermal effects** (cf Table III). Elevated temperatures obtained here are sufficient to shift the acid-base equilibrium to the right (≥ 100°C) and to accelerate the subsequent alkylation whatever heating system is.

Alkylation of Terephthalic Acid

It constitutes a more difficult case of interest to be improved as very few publications exist due to the lack of reactivity. Even with very reactive alkylating agent such as benzyl chloride, its reaction need harsh conditions (130°C)[17]. In the case of long chain halides the reactivity fails terribly as, under solvent-free PTC which is however a very efficient method, yield is limited to 17% with n-octyl bromide after 80 hours at 85°C.



The previous results with substituted aromatic compounds were then extrapolated to terephthalate considering both methods A and B under microwave or by conventional heating (Table IV)

-Table IV -

Synthesis of di n-octyl terephthalate under solvent-free PTC in a microwave oven (MW, 600W) or in an oil bath (Δ)

Molar ratio a)	Method A (MW)			Method B (MW)			Method B (Δ)		
	time min	T °C	yield %	time min	T °C	yield %	time min	T °C	yield %
1 : 2 : 2 : 0.2	7	220	67	6	166	38		–	
1 : 2.5 : 2 : 0.3	**7**	**227**	**92**	**6**	**175**	**84**	**6**	**175**	**20 b)**

a) Substrate : n $C_8H_{17}Br$: K_2CO_3 : TBAB

b) Completion to 100 % = starting materials

Excellent yields were obtained by both methods, with better results when a slight excess of n-octyl bromide was employed. **This result (84-92 %) constitutes a radical improvement for this synthesis. It is essentially due to a large specific effect of microwaves as yields not exceed 20 % with conventional heating in the same conditions.**

It is interesting to notice that such an intrinsec effect of microwaves occurs in the most difficult case as yet observed for other types of solvent free reactions[19-23]. Such an observation is coherent with a remark of D.A. Lewis[24] who underlined a generalization which have become obvious recently, stating that "slower reacting systems tend to show a greater effect under microwave radiation than faster reacting systems".

Experimental Part

Exposition of reaction mixtures was performed using a domestic microwave oven Philips AT 5964 whereas thermal measurements of substrates under microwave were carried out with a monomode reactor Synthewave 402 from Prolabo.

„ Method A

To 10 mmoles of potassium carboxylate were added in a pyrex flask 10 mmoles of n-octyl bromide and 1 mmole of tetraalkylammonium salt (Aliquat 336 or NBu_4Br). After shaking, the flask was introduced in the microwave oven (or in an oil bath for control experiments) for the indicated time. The temperature was measured by introducing a Quick digital thermometer in the sample just at the end of each irradiation. Organic products were recovered by a simple elution with 50 ml diethyl ether or methylene chloride and subsequent filtration over Florisil to remove mineral salts and catalyst. Products were analyzed by gc, characterized by ^{1}H and ^{13}C NMR, IR and MS after purification.

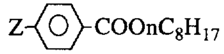
„ Method B

In a 50 ml pyrex flask were introduced 10 mmoles of carboxylic acid, 10 mmoles of finely ground base (K_2CO_3 generally) and 1 mmole of quaternary ammonium salt. After 5 minutes shaking, 10 mmoles n-octyl bromide were added. The procedure remained subsequently the same as above.

Analyses

All octyl esters were analyzed by gas chromatography using an internal standard. The column we employed is an OV1-15 m capillary one on an apparatus Carlo Erba CG 6000 (flame ionization) ; gas carrier = He (4 kbar) ; Temperatures (injector and detector) : 250°C.

Programmation in temperature = 100-180°C (10°C/min) - Retention times (rt) :



Z = NMe_2, rt = 11.35 min ; Z = OMe, rt = 9.22 min ;

Z = CN, rt = 8.49 min ; Z = NO_2 , rt = 9.33 min ; Z = H, rt = 6.40 min.

Dioctylphthalate (90 - 250°C) : rt = 18.18 min

All IR and NMR spectra were consistent with assumed formulas and (or) autentic samples[18].

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