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ALKYLATION OF POTASSIUM ACETATE IN "DRY MEDIA" THERMAL ACTIVATION IN COMMERCIAL MICROWAVE OVENS

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Abstract: Microwave irradiation using commercial domestic ovens is very efficient to activate potassium acetate on alumina in the absence of solvent ("dry media") giving rise to remarkable rate enhancements in alkylation reactions with long chain halides . These reactions can be performed quantitatively on appreciable amounts of materials in open standard pyrex vessels.

Introduction

Microwave irradiation as efficient thermal energy source is becoming a standard technique in various fields of chemistry[1]. Nevertheless, it is only recently that microwave ovens have been applied to organic synthesis[2-14].

Spectacular results have been obtained giving clear indications on the potentialities and advantages of this new technique when compared to conventional methods. It was thus shown that a great number of organic reactions (nucleophilic substitutions, esterifications, rearrangements, Diels-Alder, Claisen and ene reactions, etc..) can be considerably accelerated when conducted in commercial microwave ovens. It was generally concluded that performing reactions in such conditions resulted in faster and cleaner reactions due to less thermal decomposition of products and minimization of secondary processes[15-23].

Nevertheless, these procedures are strongly limited by the presence of solvents which reach their boiling points within very short times (≃ 1min) of exposure to microwaves[2-5]. Consequently, high pressures are developed, thus leading to damages to vessels, materials or microwave oven itself and occasionally to explosions[2-5]. These inconvenients are partially avoided by an appropriate modification of the reaction vessels (special sealed Teflon bottles) and by a limitation of the amounts of materials (about 10% of the container volume). Anyway, safety problems will limit the use of this new synthesis method.

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Using reagents supported on inorganic solid materials in the absence of solvent ("dry media" conditions) together with microwave irradiation leads to good results under very simple and safe conditions[12-14]. In addition, the main advantages of microwave irradiation are remained.

This paper describes the main advantages of dry media microwave irradiation. This technique can be applied to fair-sized samples under simple (standard open vessels in commercial domestic ovens) and safe conditions (due to the absence of solvent). Results will concern potassium acetate alkylation with long chain halides (known as poor electrophiles) performed on alumina as a solid inorganic support.

$$CH_3COOK + R\text{-}X \xrightarrow[\text{microwave}]{\text{alumina}} CH_3COOR + KX$$

$$R = nC_8H_{17},\ nC_{16}H_{33} \qquad X = Br,\ Cl$$

For the sake of clarity, the thermal behaviour of alumina alone, then of the pure reagents, finally of reagents impregnated on alumina, in microwave ovens, will be examined.

ALUMINA AND REACTANTS THERMAL STUDIES

Domestic microwave ovens are equipped with multimode cavities. The distribution of electromagnetic waves is non homogeneous; therefore to get reproducible results, it is necessary to accurately place the samples inside the oven. Furthermore, microwave effects are connected with the shapes and sizes of irradiated samples. So, the best is to use simple shaped vessels (cylindrical, spherical or cubic ones), the optimal dimensions (height and diameter) range from λ to $\lambda/10$[1,24] for the 2450 MHz domestic microwave oven with λ = 12.2cm.

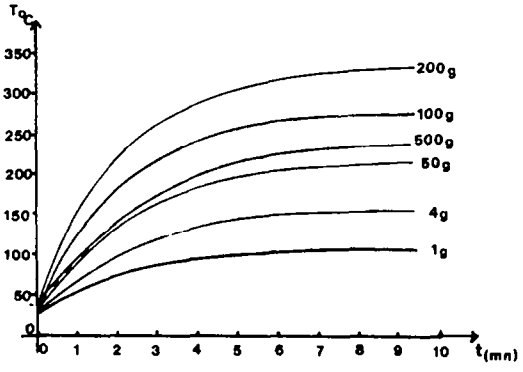
I - THERMAL BEHAVIOUR OF NEUTRAL ALUMINA

Some oxides such as alumina and silica slightly absorb microwaves at the 2450 MHz frequency[13,16,18]. This absorption has been assigned to the water molecules or hydroxyl groups present on the surface of these inorganic solids[13], but it could also be related to the non-stoichiometry character of these materials[18].

Studies of thermal behaviour of neutral alumina (Figures I and II) indicate that the temperature reached depends on the quantity of irradiated solid. A maximum, connected with the optimal capacity of the oven, is obtained for about 200 g alumina. It is to be noticed that a minimum amount of 4g is necessary to observe an appreciable thermal effect; this observation seems to confirm that the dimensions of the irradiated samples must be larger than $\lambda/10$.

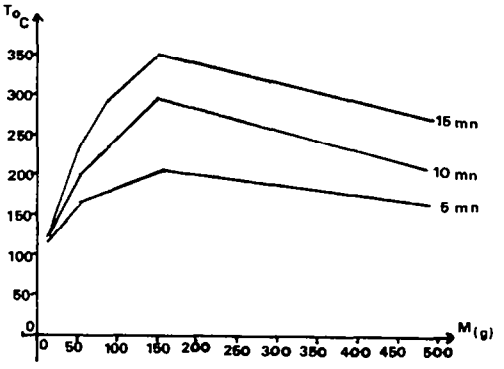
We have observed that a 1g alumina sample cannot reach more than 100°C (Figure I), even with larger irrradiation times (20mn). In these conditions, considerable energy losses cause overheating of the inner walls of the oven and of the Pyrex vessels. This could lead to irreversible damages of the magnetron .

Furthermore, during the first minutes, the temperature of the various samples (from 4g to 500g) does not change much; it remains less than 200°C. After this induction period, large temperature differences appear depending on the amount of irradiated solid. It must also be mentionned that this thermal effect diminishes when the incident microwave power is reduced.



- Figure I -

Thermal behaviour of neutral alumina (T90 Merck) as a function of the irradiation time and of the alumina amount (P=600W)



- Figure II -

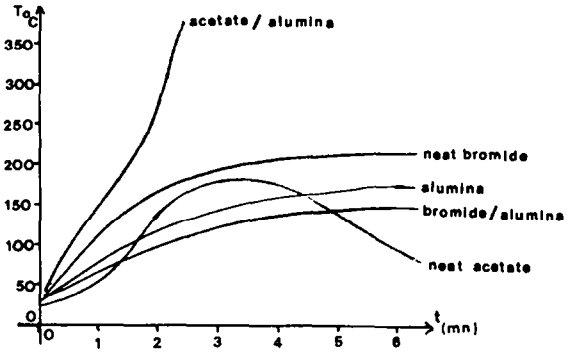
Thermal behaviour of various amounts of neutral alumina for different irradiation times (P=600W)

II - THERMAL BEHAVIOUR OF EACH REACTANTS

The behaviours of each reactant, first neat and then impregnated on alumina, under microwave irradiation, will be successively investigated.

Neat potassium acetate, after having lost water by dehydratation, which induces a temperature increase, absorbs only slightly microwave energy. It behaves as a weakly polar compound, probably because of its compactness in the solid state (tridimensional aggregates).

On the other hand, when impregnated on alumina, this compound (potassium acetate /alumina = 1/5 w/w) absorbs microwave strongly as the temperature becomes difficult to control (temperature runaway) and largely exceeds 400°C after a few minutes of irradiation (Figure III). This strong increase in temperature, i.e. of microwave absorption, is probably due to variations in the dielectric properties of the medium[1,3,11] in relation to specific interactions between alumina and potassium acetate. Thus, alumina seems to be able to induce some disaggregation, and even a partial ionic dissociation, of potassium acetate. This phenomenon could be the origin of anionic activation of this salt on the alumina surface[25].



- Figure III -

Behaviour of each reagent, alone and impregnated on alumina (4g samples, P=600W)

The absorption of electromagnetic wave by pure liquid n-octyl bromide is slightly higher than that of solid potassium acetate, probably as a consequence of its fluidity which facilitates heat transmission by convection and conduction. When impregnated on alumina, octyl bromide has almost no influence on temperature (cf Figure III).

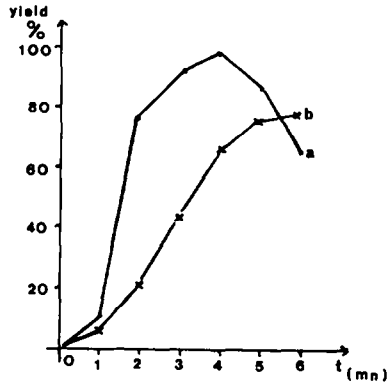
REACTION OF POTASSIUM ACETATE WITH OCTYL BROMIDE

$$CH_3COO^-K^+ + nC_8H_{17}Br \xrightarrow[\text{microwave}]{\text{alumina}} CH_3COOnC_8H_{17} + KBr$$

In a previous communication[12], we have studied this reaction, showing that microwave irradiation leads to yields comparable to those obtained by means of classical heating (i.e. oil baths)[27] but with significant reductions in reaction times (X30). The energy distribution inside the oven had not been taken into account and the amounts of reactants (about 1g of supported reagents) being too low, so that the microwave influence was rather limited and results were poorly reproducible.

I - SMALL QUANTITIES (≤1g) : USE OF AN EXTERNAL BATH OF ALUMINA

In order to overcome these drawbacks and when only small amounts can be used, we propose to use an external bath of about 200g of alumina (cf Figure II) . This bath allows a fast heating of the reaction mixture, previously placed at its center in an individual Pyrex vessel; the reaction can then occur at temperatures lower than the boiling points of the products. Reaction activations are amplified and magnetron deterioration hazards are much lower.



- Figure IV -

Effect of an external alumina bath
CH_3CO_2K support (1/5) = 1g
nOctBr = 0.17g
a) external bath (200g)
b) without bath

Under such conditions, after a 3-4 minutes irradiation at 600W, yields are improved to 92% (Figure IV) with high reproducibility. When compared to classical heating, rates are multiplied by at least 100[27].

Very accurate conditions are needed to obtain good results as fast temperature increases can induce a vaporization of the octyl acetate produced.

Such a technique offers new perspectives for efficient and safe microwave-induced organic synthesis when either small amounts are concerned or when non absorbing reactants are involved[28].

II - REACTIONS ON LARGEST QUANTITIES

As previously pointed out, optimization and reliability of microwave effects demand that the minimal dimensions of the irradiated samples are at least equal to $\lambda/10$ with λ = 12.2cm. To fulfill these conditions, reactions are performed with high amounts of reactants (at least 4g. of AcOK-alumina 1/5 mixtures) in cylindrical Pyrex open vessels whose minimal dimensions are 18 mm diameter and 12mm height.

a) Potassium Acetate in excess

When the reaction is performed with an excess of CH_3COOK with respect to nOctBr, the best yields are about 80% after 2 minutes irradiation with a 600 W power. A longer irradiation induces a large decrease in yield (only 36% after 4mn) due to vaporization of the octyl acetate produced, because the local temperature is much higher than its boiling point. This phenomemon is connected with uncontrolled temperature increase induced by a CH_3COOK/alumina excess, an effect which is represented on Figure III.

These conditions can be partly improved by a decrease in oven power: a 87% yield can be obtained in 10 minutes with a power equal to 270W.

b) Octyl bromide in excess.

In order to avoid difficulties induced by uncontrolled heating related to excess potassium acetate, we used a slight excess of alkylating agent. From the results obtained (Table I), quantitative yield is reached within two minutes of irradiation, 150 times faster than with conventional heating.

- TABLE I -

Microwave Activation (600W) in presence of excess nOctBr
CH_3COOK/alumina = 3g (5mmoles CH_3COOK)
nOctBr = 1.45g (7.5 mmoles)

time (mn)	1	1.5	2	3
final temperature (°C)	182	192	196	184
yield* (%)	63	91	99	98

*yields evaluated by gc.

In order to specify the origin of the microwave effect, the reaction was then performed in an oil bath at 190°C (i.e. very close to microwave conditions). Yields thus obtained were 0%, 13% and 80% after 2, 5 and 15 minutes respectively.

Comparison between yields after 2 minutes of reaction under microwave or classical heating suggests that the special reactivity observed under microwave activation is not due only to heating effects. As previously suggested[13], this observation can be related to the poor thermal diffusion of alumina which is a barrier for thermal activation of the reaction whereas microwaves are easily transmitted. However, further work is necessary.

After optimization of the reaction, we have tested the reproducibility of the results and looked for the possibility of operating on larger amounts of reagents. We have found yields ranging from 95 to 99% for six experiments. We have obtained the same yields when largest amounts of reagents were involved (from 5 to 100 mmoles of potassium acetate). For instance, a yield of 99 % was obtained within 2 minutes of irradiation on 0.1 mole (9.8g) of CH_3COOK impregnated on 40g alumina reacting with 0.15 mole (29g) of n-octyl bromide.

c) Comparison between impregnated and dispersed acetate.

In order to test the possibility of using simply dispersed potassium acetate in alumina without previous impregnation, we have performed a series of experiments with such reagents (Table II).

- TABLE II -

Microwave activation (600W) for the reaction with dispersed acetate on alumina
CH_3COOK = 5 mmoles ; alumina = 2.5g ; nOctBr = 6 mmoles

time (mn)	1	2	3	4	5	10
final temperature (°C)	167	172	161	152	146	140
yield (%)	12	26	51	58	67	66

By comparing the results (Tables I and II), it appears that impregnated acetate reactivity is much higher than that of dispersed species. Such a behaviour has already been underlined with CH_3COOK[29], but also with KCN[30], NaCN[31] and NaOH[32].

ALKYLATION WITH HEXADECYL HALIDES

$$CH_3COOK + C_{16}H_{33}X \xrightarrow[\text{Microwave}]{\text{Alumina}} CH_3COOC_{16}H_{33} + KX$$

X= Br or Cl

Microwave activation was also studied in the case of acetate alkylation by halides with longer chains, and consequently less reactive. We have thus tested hexadecyl bromide (bp = 305°C) and chloride (bp = 260°C).

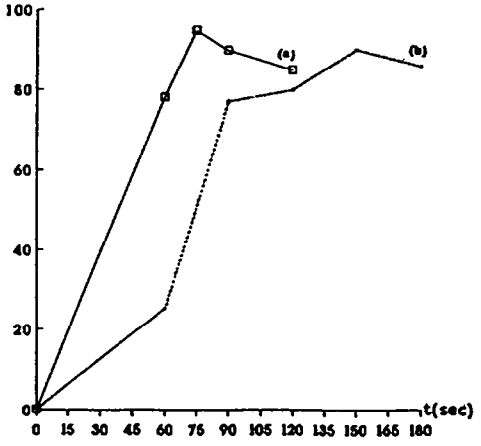
I - HEXADECYL BROMIDE

We have first used the conditions of octyl bromide reaction. Reaction is incomplete and yields remain constant, near 80%, after 2, 3 and 4 minutes of irradiation.

Further studies were necessary to improve these results (Figure Va). Thus, it is possible to reach 95% yield after only 75 seconds of irradiation if reaction is carried out in presence of an excess of CH_3COOK. This rate enhancement (300 times with respect to conventional heating) is essentially due to potassium acetate excess which induces a fast increase of temperature and consequently an improved reactivity.

II - HEXADECYL CHLORIDE

Chlorinated alkylating agents are usually less reactive than their corresponding brominated ones. Nevertheless, as they are cheaper and more readily available, they are of great interest in organic synthesis[33]. So, we have studied their behaviour under microwave irradiation (Figure Vb).



- FIGURE V -

Microwave Activation (600W) of the reaction : $CH_3COOK + C_{16}H_{33}X$
CH_3COOK/alumina = 4.5g (7.5 mmol. CH_3COOK)
$nC_{16}H_{33}X$ = 5 mmol.
a) X = Br : Final temperature = 234°C
b) X = Cl : Final temperature = 275°C

In these conditions, chloride reactivity is only slightly lower than that of bromide compounds. A 90% yield can be reached after 2.5 minutes of irradiation whereas yield is zero after 20 hours at 85°C with conventional heating. So, chlorinated alkylating agents can easily be used in the reaction, which is not the case usually.

Conclusions

Excellent yields (90-99%) can be obtained in the synthesis of long chains alkyl acetates by microwave irradiation of solvent-free reaction media. Reaction times are very short (generally less than 3 minutes) and rates can be as high as 300 times than those obtained with conventional heating. Appreciable amounts of reagents can be involved (0.1 mole or more) in safe and easy conditions. When only small amounts of products are available (about 1 gram), the use of an external alumina bath is highly beneficial.

The experiments described here show clearly that the use of microwave ovens for rapid solvent free organic synthesis, either on solid supports in " dry media"[13,14] or by solid-liquid phase transfer catalysis without solvent[34], is of great interest. Difficult thermal reactions can be performed rapidly in safe conditions, in particular when high boiling point products are involved.

It seems that the microwave effect is essentially connected with specific heating effects[5]. However, when supported reactions are concerned, this effect alone cannot explain the special reactivity under microwave irradiation.

Experimental part

Equipment

All experiments were performed in a 2450 MHz commercial oven, a AVM705 Philips model. It is fitted with a mixing wire, a precise digital time-switch and a power selector from 125 to 600 W. A coarse temperature measurement is performed by introducing a Quick digital thermometer in the sample just at the end of each irradiation; in these temperature determinations, variations between several readings are less than 5°C.

Oven cartography

Hot zones of the oven are previously delimited by using a wet blotting-paper that, after a short irradiation, allow to localize the zones of maximal electric field (burnt parts of the irradiated paper). Then, the sample to be irradiated is placed at a hot point of the oven, always at the same place.

General procedure

Impregnated potassium acetate on alumina is prepared by mixing solid alumina with an aqueous solution of the salt, then by removing water under reduced pressure. Reagents mixtures (impregnated acetate and neat alkyl halides) are introduced in open cylindrical Pyrex vessels. After irradiation, the mixtures are cooled to room temperature and then simply eluted with an organic solvent (diethyl ether or methylene chloride). Organic compounds (alkyl acetates and halides) are then analyzed by gc using an internal standard and by NMR[29].

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REFERENCES

1. Thuery,J.;"Les microondes et leurs effets sur la matière",Technique et Documentation-Lavoisier,1989,2nd edition.
2. Gedye,R.N.;Smith,F.E.;Westaway,K.C.;Ali,H.;Baldisera,L.;Laberge,L.;Rousell,J. *Tetrahedron Lett.*1986, *27*,279-282.
3. Giguere,R.J.;Bray,T.L.;Duncan,S.M.;Majetich,G. *Tetrahedron Lett.*1986, *27*,4945-4948.

4. Giguere,R.J.;Namen,A.M.;Lopez,B.O.;Arepally,A;;Ramos,D.E.;Majetich,G.;Defauw,J. *Tetrahedron Lett.*1987, *28*,6553-6556.
5. Gedye,R.N.;Smith,F.E.;Westaway,K.C. *Can.J.Chem.*1988, *66*,17-26.
6. Linders,J.T.M.;Kokje,J.P.;Overhand,M.;Lie,T.S.;Maat,L. *Recl.Trav.Chim.Pays-Bas*, 1988, *107*,449-454.
7. Takano,S.;Kijima,A.;Sugihara,T.;Satoh,S.;Ogasawara,K. *Chem.Lett.*1989,87-88
8. Straathof,A.J.J.;Van Bekkum,H.;Kieboom,A.P.G. *Recl.Trav.Chim.Pays-Bas*,1988, *107*, *647-648*.
9. Chen,S.T.;Wu,S.H.;Wang,K.T. *Int.J.Pept.Prot.Res.*,1989, *33*,73-75.
10. De La Guardia,M.;Salvador,A.;Gomez,M.J.;De Benzo,Z.A. *Anal.Chim.Acta*,1989, *224*, 123-126.
11. Giguere,R.J. in "Organic Synthesis: Theory and Applications"; Hudlicky,T. edit., Vol.1,1989,153-172,JAI Press, London.
12. Gutierrez,E.;Loupy,A.;Bram,G.;Ruiz-Hitzky,E. *Tetrahedron Lett.*,1989, *30*,945-948.
13. Ben Alloum, A.;Labiad,B.;Villemin,D. *J.Chem.Soc.,Chem.Commun.*,1989,386-387.
14. Villemin,D.;Labiad,B.;Ouhilal,Y. *Chem. & Ind.*,1989,607-608.
15. Fisher,L.B. *Anal.Chem.*,1987,1799-1800.
16. Walkiewicz,J.W.;Kazonich,G.;McGill,S.L. *Minerals and Metallurgical Processing*,1988, *5*,39-42
17. Thuillier,F.M.;Jullien,H.;Grenier-Loustalot,M.F. *Makromol. Chem., Macromol. Symp.* 1988, *9*,57-68.
18. Baghurst,D.R.;Mingos,D.M.P. *J.Chem.Soc.,Chem.Comm.*,1988,829-830.
19. Sun,W.C.;Guy,P.M.;Jahngen J.H.;Rossomando,E.F.;Jahngen,E.G.E. *J.Org.Chem.*,1988, *53*, 4414-4416.
20. Yu,H.M.;Chen,S.T.;Chiou,S.H.;Wang,K.T. *J.Chromatogr.*,1988, *456*,357-362.
21. Baghurst,D.R.;Mingos,D.M.P.;Watson M.J. *J.Organometal.Chem.*,1989, *368*,C43-C45.
22. Ali,M.;Bond,S.P.;Mbogo,S.A.;McWhinnie,W.R.;Watts,P.M. *J.Organometal.Chem.*,1989, *371*, 11-13.
23. Chiou,S.H.;Wang,K.T. *J.Chromatogr.*,1989, *491*,424-431.
24. (a)Chazeau,J.C."Risques liés à l'utilisation domestiques des fours à micro-ondes", Société de Médecine du Travail Dauphiné-Savoie, Chambéry, 1986(March 7th). (b)Malabiau,M."Interactions entre matière et rayonnement"DCAN,Toulon,1987.
25. Delmotte,M.;Jullien,H.;work in progress (Lab.OMM, Thiais).
26. (a)Foucaud,A.;Bram,G.;Loupy,A. in "Preparative Chemistry Using Supported Reagents" P.Laszlo edit., Chapter 17,Academic Press,1987,London. (b)Posner,G.H.;Ibid, Chapter 16.
27. Bram,G.;Decodts G. *Tetrahedron Lett.*,1980,5011-5014.
28. Bram,G.,Loupy,A.;Majdoub M.;Devicq,M.;Anthraquinone microwave induced synthesis, to be published.
29. Barry,J.;Bram,G.;Decodts,G.;Loupy,A.;Pigeon,P.;Sansoulet,J. *Tetrahedron*,1983, *39*, 2673-2677.
30. Bram,G.;Fillebeen-Khan,T.;Geraghty M. *Synthetic Comm.*,1980, *10*,279-289.
31. Regen,S.L.;Quici,S.;Liaw,S.J. *J.Org.Chem.*,1979, *44*,2029-2030.
32. Czech,B.;Quici,S.;Regen,S.L. *Synthesis*,1980,113.
33. Loupy,A.;Pardo,C. *Synthetic Comm.*,1988, *18*,1275-1281.
34. Bram,G.;Loupy,A.;Majdoub,M. *Synthetic Comm.*,1990, *20*,125-129.