Pergamon

*Tetrahedron*, Vol. 52, No. 2, pp. 617-628, 1996

0040-4020/96 $15.00 + 0.00

0040-4020(95)00900-0

# Coupling Focused Microwaves and Solvent-Free Phase Transfer Catalysis : Application to the Synthesis of New Furanic Diethers

**Mustapha MAJDOUB[2], André LOUPY[1]*, Alain PETIT[1] and Sadok ROUDESLI[2].**

*1- Laboratoire des Réactions Sélectives sur Supports- ICMO-Université Paris-Sud CNRS UA 478, bâtiment 410- 91405 Orsay cédex, France.*

*2- Laboratoire de Chimie des Polymères- Faculté des Sciences-5000 Monastir, Tunisie.*

**Abstract:** A new family of furanic ethers was obtained by alkylation of 2,5-furandimethanol or furfuryl alcohol under microwave in phase transfer catalysis (PTC) conditions in the absence of solvent. Products were synthesized in good yields (> 80 %) within 10 min or less. Compounds were analysed by NMR, mass spectrometry and their thermal behaviours were studied by DSC. When compared to conventional heating, everything equal elsewhere, reaction times were improved under microwave conditions at a restitute power of 30 Watts when performed under stirring in a monomode reactor (Synthewave 402 Prolabo).

**Key words:** Microwaves / monomode reactor / solid-liquid PTC without solvent / furanic ethers /O-alkylation.

## Introduction

Biomass constitutes a renewable source of natural products able to be used as unfailing starting materials for access to new compounds, less polluting and able to substitute petroleum derivatives.

Among the important derivatives of biomass, we can find furanic compounds obtained from furfural (world production = 200 000 t/year)[1]. These materials have been dealt within numerous works and their chemistry is one of the most reported [1-6].

In this study, we were especially interested in several applications of 2,5-furandimethanol (FDM) which was previously synthesized from 5-hydroxy furfural [7]. However, very few publications concern this product, essentially applying O-alkylation reactions [8-12]. This lack of interest could be due to the relative unstability of these products to light and moisture.

A main goal in our laboratories is to valorize this biomass derivative and to involve it in some polyalkylations in order to elaborate new functionalized polyethers. It aims to the synthesis of new furanic diethers under clean and easy-to-perform conditions. Thus, this work deals with O-alkylation under conditions of PTC without solvent using concomitant microwave irradiation. These coupled technologies have been proved to be very efficient methods to carry out anionic activation, especially alkylations[13-15].

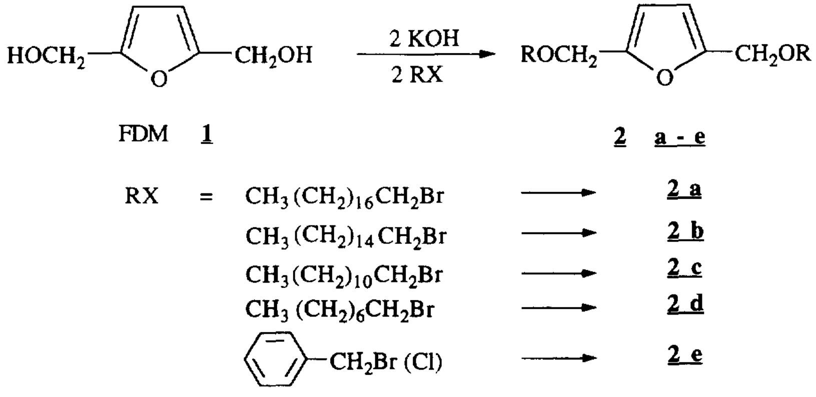
## Experimental part

### Reactants and Equipment

The different involved products are commercial (of purity > 98%) from Janssen and Aldrich. They were used without further purification excepted for 1,12-dibromododecane which was previously crystallized from methanol, and furfurylic alcohol which was distilled.

The microwave reactor is a monomode system (Synthewave 402 : prototype designed by Prolabo). The temperature is evaluated either by a Luxtron optical fiber or by infrared detector which indicates the surface temperature [17] (IR lecture was calibrated using a thermocouple introduced in the reaction mixture). Mechanical stirring provides a good homogeneity of the materials. Automatic control of the irradiation (power and temperature) as well as data treatment was followed by a computer system.

### Synthesis of furanic diethers from FDM 1 and alkyl halides (Scheme I)



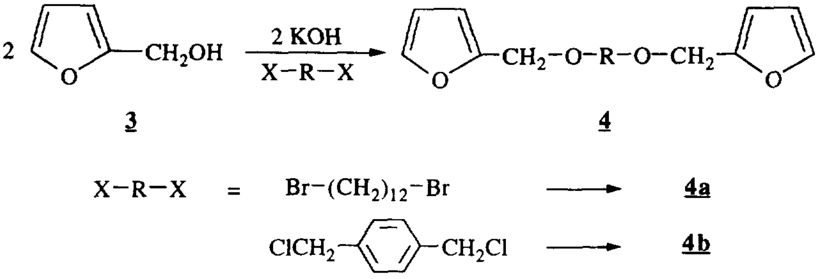
**Scheme I**

We described here the general experimental procedure in the case of reactions performed under microwave activation. In order to ensure the reaction to go to completion, a slight excess of base and alkylating agent was used relative to each one of the two hydroxyl functions of FDM (1.25 molar equiv.) in the presence of a catalytic amount of phase transfer agent.

So, in a Pyrex cylindrical reactor adapted to the Synthewave system, 10 mmoles of FDM (1.28 g) were mixed with 25 mmoles of alkyl halide, 2 mmoles of Aliquat 336 (0.808 g) and 25 mmoles of powdered KOH (1.6 g) [containing about 15% of water]. The mixture was then homogenized and submitted to monomode microwaves with mechanical stirring for the adequate time.

At the end of the reaction, the mixture was cooled down to room temperature and diluted with 20 ml of methylene chloride or diethyl ether. The solution was filtered (KOH in excess, generated salts). The filtrate was then concentrated and poured dropwise into 300 ml of methanol under intense stirring. The diethers 2 precipitate, therefore free from excess of reactants, catalyst and monoethers which are all soluble in methanol. After filtration and drying under vacuum, the product was recrystallized from adequate solvent.

### Synthesis of furanic diethers from furfuryl alcohol 3 and dihalides (Scheme II)



**Scheme II**

The experimental procedure was almost identical to the precedent one excepted that the order of introduction of reactants was modified.

To 20 mmoles of freshly distilled furfuryl alcohol (1.96g) were added 15 mmoles of powdered KOH (1g ) [containing about 15% of water].under stirring, 1 mmole of Aliquat 336 ( 0.404 g) and finally 5 mmoles of dihalide. The mixture was irradiated under microwaves with mechanical stirring. The treatment remained the same as above.

### Products analysis

All products were analysed by $^{1}H$ NMR (Bruker equipments at 250 and 400 MHz) and some of them by $^{13}C$ NMR . Spectra were in agreement with the proposed structures. As typical examples, two spectra of these models are given in Figures I and II.

**Figure I**

400 MHz $^{1}H$ NMR spectrum of 2b in $CDCl_3$

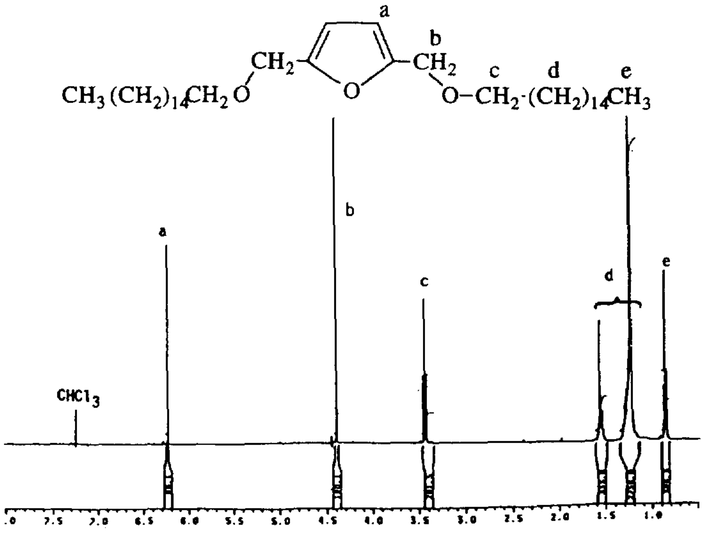
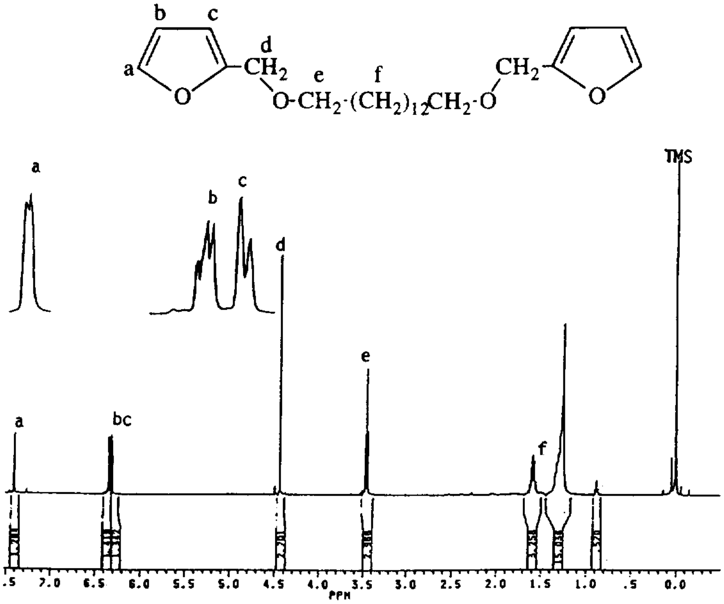


**Figure II**

400 MHz $^1H$ NMR spectrum of **4a** in $CDCl_3$



Structures and purities were confirmed by their centesimal microanalysis, mass spectrometry (chemical ionization with $NH_3$) and gas chromatography for the compounds of low molecular weights.

Finally, thermal behaviour of each model was studied by differential scanning calorimetry (DSC) on an Epson apparatus (Setaram DSC 92) and melting points were evaluated (cf. Table V) with good precision (± 0.5°C).

## Results and Discussion

### A- Synthesis of 2b as a model reaction

### 1- Determination of the best experimental conditions

In order to evaluate the best adapted conditions to be applied subsequently to microwave activation, we have considered four different possibilities involving anionic activation to promote O-alkylation. They were tested under classical conditions, i.e. under conventional heating.

Method A = solid-liquid PTC without solvent (solid KOH + Aliquat)
Method B = liquid-liquid PTC without organic solvent (aqueous KOH + Aliquat)
Method C = reaction in dipolar aprotic solvent (solid KOH in DMSO)

Method D = reaction on solid mineral support in "dry media" (previous preparation of the dialkoxide salt, then impregnation onto alumina).

The main results are brought together in Table I

### - Table I -

**Comparison between the different conditions for the synthesis of 2b under conventional heating**

Diol : 10 mmoles ; KOH : 25 mmoles ; R-X : 25 mmoles ; Aliquat : 2 mmoles.
Temperature : 85°C ; Magnetical stirring : 300 rpm.

| Entry | Method | Reaction time (h) | Yield [a] 2b (%) |
|---|---|---|---|
| 1 | A | 5 | 93 |
| 2 | B | 5 | 89 |
| 3 | C | 5 | 78 |
| 4 | D | 15 | traces |

a) Yield based on isolated product.

The best yields were obtained under PTC conditions without solvent either using powdered KOH (Method A) or aqueous KOH (method B). Using method C led to secondary reactions such as β-elimination as proved by NMR and IR, inducing thus lower yields. Reaction on alumina (method D) was quasi non-effective even by extending the reaction time. This could be due to the great heterogeneity of the system and to the dilution (or dispersion) of reactants on supports.

These preliminary results indicated clearly that the most efficient conditions involved solvent-free PTC. In order to be applied to microwaves, it was obvious that use of solid KOH has to be preferred to aqueous KOH due to the fast and unchecked evaporation of water even at a low power level.

### 2- Optimization under microwave irradiation

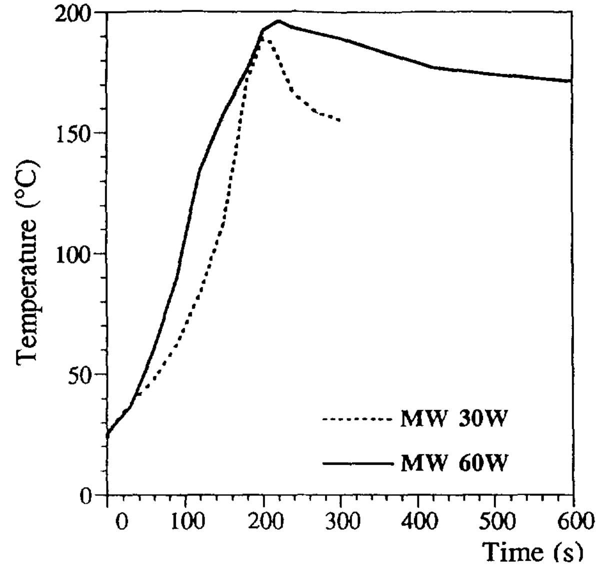
Previously to any new reaction study under microwaves, we need to test the thermal behaviour of every reactants as well as reaction mixtures when they are submitted to the electromagnetic field. This preliminary step allowed to determine adequate conditions of incident power and irradiation time. In this specific case, all materials are polar, excepted 1-bromododecane, and consequently highly subject to interact with radiations.

In a first approach, we have performed several experiments at various powers, fixing all other parameters (reaction time = 10 min ; relative amounts of reactants = 1.25 molar equivalent of KOH and RX for

**one function alcohol). The maximum reached temperatures lie in the range of 180-200°C after 3 min of exposure to microwave (Figure III).**

**Figure III**

Thermal behaviour of the reaction mixture under the optized conditions.



In other respects, the results of these experiments (Table II) have shown that yields were about 60% for all power levels.

### - Table II -

**Effect of incident power on Dialkylation of FDM (1) with 1-bromohexadecane under solvent-free PTC coupled with microwaves.**

Diol : 10 mmoles ; KOH : 25 mmoles ; R-X : 25 mmoles ; Aliquat : 2 mmoles.
Reaction time : 10 mn ; Mechanical stirring

| Entry | Power (W) | Maximum [a] temperature (°C) | Yield [b] 2b (%) |
|---|---|---|---|
| 5 | 30 | 160 | 57 |
| 6 | 60 | 170 | 58 |
| 7 | 120 | 175 | 63 |
| 8 | 180 | 185 | 56 |

a) Maximum temperature measured by IR detection.

b) Yield based on isolated product.

Afterwards, the effect of irradiation time on yields was investigated (Table III). We have established that, under these conditions, yields were not affected by the time of exposure to microwave. The best yield (69%) was obtained within 20 minutes at a power of 60 W .

### - Table III -

**Effect of irradiation time on Dialkylation of FDM (1) with 1-bromohexadecane under solvent-free PTC coupled with microwaves**

Diol : 10 mmoles ; KOH : 25 mmoles ; R-X : 25 mmoles : Aliquat : 2 mmoles.
Power : 60 W; Mechanical stirring

| Entry | Time (min) | Maximum temperature (°C) | Yield a) **2b** (%) |
|---|---|---|---|
| 9 | 10 | 170 | 58 |
| 10 | 15 | 165 | 63 |
| 11 | 20 | 175 | 69 |
| 12 | 30 | 167 | 67 |

a) Yield based on isolated product.

Finally, we have investigated the effect of variations in relative amounts of reactants 1 / KOH / RX. The main results are summarized in Table IV

### - Table IV -

**Effect of relative amounts of reactants on Dialkylation of FDM (1) with 1-bromohexadecane under solvent-free PTC conditions coupled with microwaves**

Diol : 10 mmoles ; Aliquat : 2 mmoles
Reaction time : 10 mn ; Power : 60 W ; Mechanical stirring

| Entry | KOH/Diol | RX/Diol | Yield b) **2b** (%) |
|---|---|---|---|
| 13 | 2 | 3 | 40 |
| 14 | 2.5 | 2 | 50 |
| 15 | 2.5 | 2.5 | 58 |
| 16 | 3 | 2.5 | 57 |
| 17 | 3 | 3 | 92 |
| 18 a) | 3 | 3 | 93 |

a) 30 W within 5 min.

b) Yield based on isolated product

From these results, it appeared that, in order to obtain quasi-quantitative yields (92%), it was necessary to use 1.5 molar equivalents of both KOH and RX versus alcohol functions. Liquid alkyl bromide in excess seemed to play the role of diluent by homogenizing the mixture and making easier diffusion of reactants. This effect could be noticeable at the end of the reaction when reaction mixture is becoming more viscous and heterogeneous (evaporation of water, formation of KBr).

**In conclusion, the optimal free PTC conditions involved a system consisting of diol <u>1</u> (1 eq), powdered KOH (3 eq), alkyl halide RX (3 eq) and Aliquat (0.2 eq) and irradiation by focused microwaves within 5 to 10 min at low power levels (30 or 60 W).**

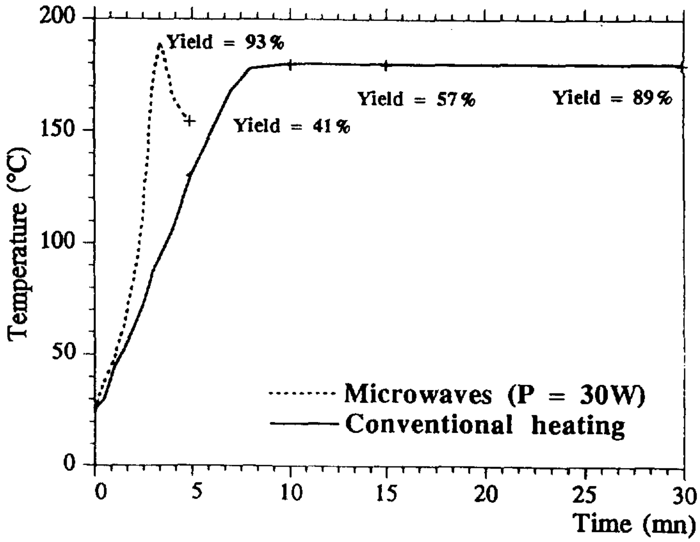
In other respects, the profile of the curve temperature as a function of irradiation time could give valuable indications on the evolution of the reaction and the detection of its end. For instance, figure III represented thermal evolutions in experiments 17 and 18 under microwave; the maximum temperature (around 190°C) was significant of consumption of polar molecules and consecutive decrease in the curve indicative of formation of less polar species.

## 3- <u>Comparison between conventional heating and microwave activation</u>

A series of experiments were performed in an oil bath at 180°C. In order to get the more serious comparisons, we have recorded thermal evolutions of reaction medium as a function of time and evaluated yields obtained after various times (Figure IV).

<u>Figure IV</u>

Synthesis of <u>2b</u> : Comparison between microwave and thermal conditions.



**A clear improvement of the reaction was observed under microwave conditions in the same range of temperature. For instance, it needs 30 minutes to obtain 89% yield by conventional heating whereas 93% was attained within 5 minutes of microwave irradiation at a power of 30 W.**

We could notice that the elevation rate in temperature was higher under microwave. This rise could be at the origin of acceleration[18] as well as a better homogeneity in temperature and possible modifications of activation parameters ($\Delta H^{\#}$ and $\Delta S^{\#}$)[19]. However, these interpretations lie necessarily on comparisons based on macroscopic temperatures and we could always ask ourself if they are effectively representative of what happens at the molecular stage (cf. hot spot theory).

### B- Extension to other furanic diethers 2a-2e

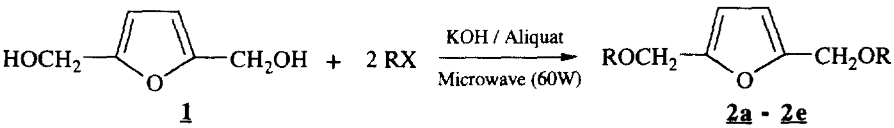
We have extrapolated these optimized conditions to the synthesis of a series of new furanic diethers with aliphatic or aromatic chains 2a - 2e (Table V).

**- Table V -**

**Dialkylation of FDM (1) with alkyl or benzyl halides under microwaves under solvent-free PTC conditions**

Diol : 10 mmoles ; R-X : 30 mmoles ; KOH : 30 mmoles ; Aliquat : 2 mmoles

Microwave power : 60 W ; Irradiation time : 10 mn ; Mechanical stirring



| Entry | Product | T max (°C) | Yield a) (%) | purification | m.p. d) (°C) |
|---|---|---|---|---|---|
| 17 | 2b | 196 | 92 | crystallization from MeOH/CHCl3:4/1 (v/v) | 61 |
| 19 | 2a | 198 | 81 | crystallization from MeOH/CHCl3:3/1 (v/v) | 63 |
| 20 | 2c | 180 | 94 | crystallization from MeOH | 47 |
| 21 | 2d | 172 | 93 b) | Distillation (180-185°C) at 1mm Hg | 9 |
| 22 c) | 2e | 105 | 74 | crystallization from n-pentane | 44 |

a) Yield based on isolated product. b) Determinated by G.C.

c) System = aqueous KOH /Aliquat (method A). Maximum temperature (imposed) = 100°C ; time = 5 mn.

d) Melting points determined by DSC from -20°C to 150°C with an elevation rate in temperature of 10°C/mn.

**Long chain diethers (from $C_8$ and $C_{18}$) were obtained in good yields (81-93%) within 10 mn at 60 W. These compounds are stable, easy to isolate and to purify.**

On the other hand, benzylic diether is more unstable and could not be obtained simply under the same conditions. It could be synthesized with a satisfactory yield (74%) under milder conditions using aqueous KOH (method B) at a temperature ≤100°C.

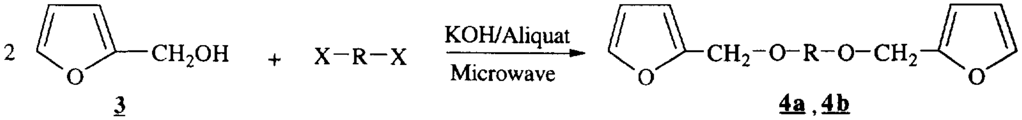
C- Alkylation of furfurylic alcohol by dihalides (Table VI)

**We have synthesized two new diethers under the same experimental conditions as previously described. Yields were excellent within 10 minutes of irradiation at 60 W. These compounds are stable, easy to isolate and to purify.**

**- Table VI -**

**Alkylation of furfuryl alcohol 3 by dihalides**

Alcohol : 20 mmoles ; KOH : 15 mmoles ; X-R-X : 5 mmoles ; Aliquat : 1 mmole
Microwave power = 60 W ; Irradiation time = 10 min ; Mechanical stirring.



| Entry | Product | $T_{max}$ a) (°C) | Yield b) (%) | purification | m.p. c) (°C) |
|---|---|---|---|---|---|
| 23 | 4a | 170 | 96 | crystallization from acetone / water: 2/1 (v/v) | 47 |
| 24 | 4b | 172 | 78 | crystallization from MeOH/water: 2/1 (v/v) | 44 |

a) Maximum temperature during the experiment (IR detection). b) Yield based on isolated product.
c) Determinated by heating microscope.

## Conclusion

In this article, we have defined optimal situations to synthesize in a one-step procedure furanic ethers under microwaves within less than 10 min under mild, clean, and efficient conditions. So, we have elaborated several new diethers from furanic derivatives and poorly reactive long chain halides. Thus, we have demonstrated that solvent-free PTC is the most suitable technique for this kind of reaction under microwaves, under non-polluting and efficient conditions. On the other hand, this study led to a better understanding of alkylation of furanic derivatives, which can now be used to elaborate new functionalized polyethers by reacting FDM and dihalides.

**Acknowledgements:** Support for this work has been provided by the " Coopération Scientifique et Universitaire Franco-Tunisienne ( CMCU)". Our sincere thanks are due to Claude Merienne for NMR assistance and stimulating discussions.

## References

1. Gandini, A.; Encyclopedia of Polymer Science on Engineering. J. Wiley Edit., New-York **1986** , 7,454.
2. Dunlop, A.P.; Peters F.N.; The Furans. Am. Chem. Soc. Series N° 119. Reinhold Publishing Corp., New-York **1953**.
3. Gandini, A. Comprehensive Polymer Science. First supplement. Pergamon Press, Chapter **1992**, 19 , 527.
4. Gandini, A. A. C. S. Symp. **1990** Series N° 433, 195.
5. Sergent, M.V.; Cresp, T.M. "Furans" in D. Barton and W. D. Ollis ed. Comprehensive Organic Chemistry, Pergamon Press, Oxford **1979**, 4 , 639.
6. Mc Killip, W.J.; Sherman E. "Furans Derivatives" in M. Grayson, edit K. Othmer. Encycl. of Chemical Technology, J. Wiley, New-York. **1981**, 11 , 499-527.
7. Blanksma, J. J. Rec. Trav. Chim. Pays-Bas, **1910**, 29 ,403-406.
8. Tinko, J.M.; Cram, D.J. J. Am. Chem. Soc., **1974**, 96, 7159-7160.
9. Gray, R.T.; Reinhoudt, D. N.; Smit C.J.; Veenstra Ms.I. Rec. Trav. Chim. Pays-Bas **1976**, 95, 258-263.
10. Sorokin, V. P.; Moshchinskaya, N. K. USSR Patent (1966) 188.022; C.A. **1967**, 67, 74130 x .
11. Sorokin, V. P.; Moshchinskaya, N. K. USSR Patent (1968) 209.740; C.A. **1968**, 69 , 19992 w.
12. Moore, J.A; Kelly, J. E. Polymer Prep., Am. Chem. Soc., Div. Polym. Chem. **1974**, 15 (2), 77-81.
13. Bram, G.; Loupy, A.; Majdoub, M. Synthetic Commun. **1990**, 20, 125-129.
14. Barnier, J. P.; Loupy, A.; Pigeon, P.; Ramdani, M.; Jacquault, P., J. Chem. Soc. Perkin Trans I,**1993**, 397-398.

15. Loupy, A.; Petit, A.; Ramdani, M.; Yvaneff, C.; Majdoub, M.; Labiad, B.; Villemin, D.; Can. J. Chem. **1993**, 71, 90-95.

16. Commarmot, R.; Didenot, R.; Gardais, J. F. French Patent Rhône-Poulenc / Prolabo **1986**, N°84/03496 (27-10-86).

17. Jacquault, P. European Patent **1992**, N°549 495 AI (21-12-92)

18. Stuerga, D.; Gonon, K.; Lallemant, M. Tetrahedron **1993**, 49, 6229-6234.

19. Lewis, D. A.; Summer, J. D.; Ward, T. C.; Mc Grath, J. C. J. Polymer Science Part A **1992**, 30, 1647-1653.

(*Received in Belgium* 24 *July* 1995; *accepted* 2 *October* 1995)