Synthesis of π-Conjugated Systems from Methyldiazines and Aromatic Aldehydes under PTC Conditions and without Organic Solvent

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Abstract: The condensation reactions of 4-methylpyrimidine and methylpyrazine with *p*-anisaldehyde have been studied in NaOH 5M in the presence of catalytic amount of a quaternary ammonium salt ("quat"). This study seems to give credit to a PTC/OH extraction process where an hydroxide ion would be transferred into the "pseudo organic phase" consisted by liquid reagents. However, an IPTC process cannot be ruled out for some of tested quats.

Keywords: Methyldiazines, Condensation reactions, Reactions in aqueous medium, Quaternary ammonium salts, Phase transfer catalysis, Inverse phase transfer catalysis.

INTRODUCTION

Condensation reactions of organic compounds possessing active methyl or methylene groups on aromatic aldehydes appear among the procedures the most used to form a new carbon-carbon bond. Such reactions proceed in an initial step by the formation of a carbanion. This step is generally easy from methylene groups located between two electron-withdrawing substituents (e.g. from acetylaceton) and the action of a weak base as piperidine is sufficient to produce the corresponding carbanions. The situation is more delicate from precursors having methylene or methyl group of weaker acidity (e.g. acetophenone). In this case, the following experimental conditions are generally required: (i) action of strong bases in organic solvents [1-2], (ii) use of NaOH in hydroalcoholic medium [1-2], (iii) recourse to phase transfer catalysis (PTC) in biphasic medium [3].

In the last two decades, the increasing necessity to limit, as far as possible and for environmental reasons, the use of organic solvents to transform chemicals has led to the development of water as medium for many organic reactions [4-7]. Aldol condensations and related syntheses (Knoevenagel, Michaël, ...) also took advantage from this synthetic strategy [8-14] and the most widely reported experimental conditions are, for these reactions, the use of a diluted solution of NaOH without organic solvent but in presence of a catalytic amount of a quaternary ammonium salt. The catalytic activity of such ammonium salts is due to their capability to enhance the solubilization of organic reagents in aqueous phase but can also be related to a micellar catalysis: indeed, some quaternary ammonium salts (e.g. cetyltrimethylammonium bromide) form, above the CMC (critical micellar concentration), micellar aggregates in aqueous medium and lead to an increase of the local concentration in reagents in close vicinity to these micelles. The combination of these two factors has been named by Boyer *et al.* "inverse phase-transfer catalysis" (IPTC) [15]. Furthermore, the same authors recently showed that this IPTC process is mainly effective under low stirring rates, whereas an interfacial mechanism is proposed to occur under higher stirring rates [16].

We have recently demonstrated that (di)methyldiazines, despite the poor activation of the aliphatic C-H bonds in such compounds, readily react with aromatic aldehydes in a hot aqueous solution of sodium hydroxide 5 M, in the presence of a catalytic amount (10 % mol) of a quaternary ammonium salt and in absence of any organic solvent, to afford the expected condensation compounds (see Fig. **1**) [17]. This

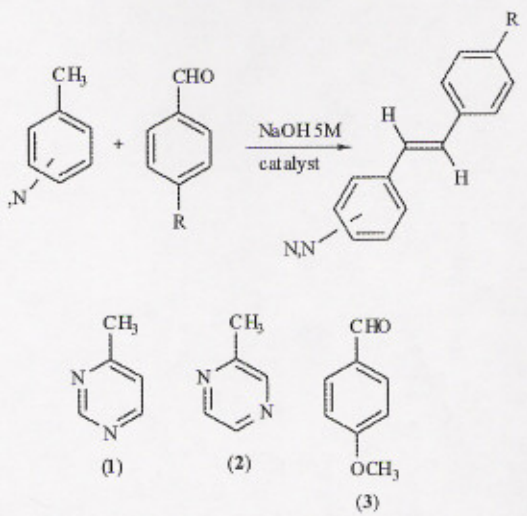

Fig. (1). Experimental protocol and reagents 1– 3.

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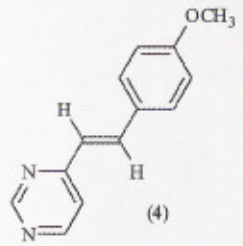
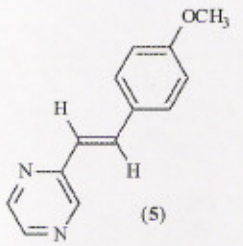


(4)



(5)

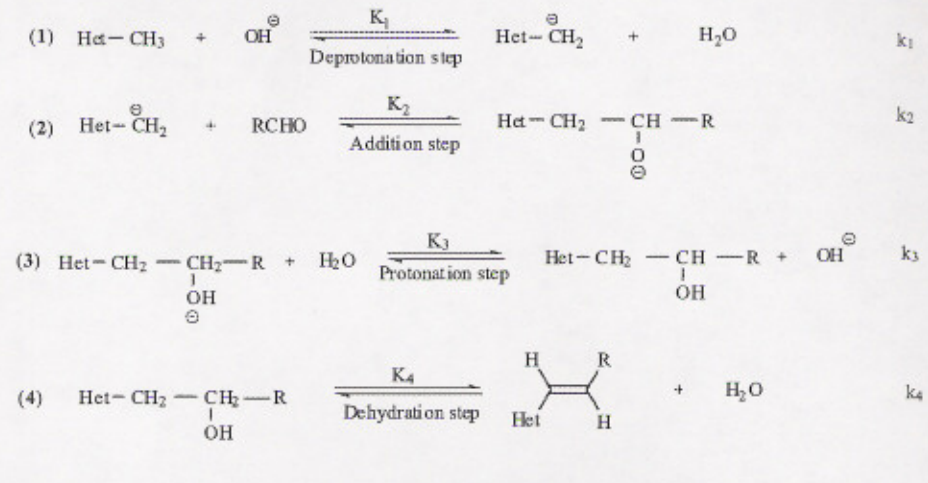


Fig. (2). Conjugated systems **4** – **5** and overall mechanism of the condensation reaction.

experimental procedure allowed us to prepare new conjugated systems containing three aromatic cycles and derived from oligo(phenylenevinylene)s. Electronic and optical properties of such compounds could be tuned over a large energy range by a tailored design of the molecular structures [18].

The aim of this work is to approach the mechanism of the reaction and to understand the catalytic action of the quaternary ammonium salt. Two model reactions have been studied: the reactions between 4-methylpyrimidine (**1**) or methylpyrazine (**2**) and *p*-anisaldehyde (**3**) (Fig. **1**).

RESULTS AND DISCUSSION

1. Determination of the Rate-limiting Step

It is well known that aldol condensations proceed by the general reaction scheme shown in Fig. (**2**) in the case of reactions proceeding from methyldiazines; the four steps featuring a priori as equilibrium situations. The first objective of this study was to determine, for the two studied reactions, the rate-limiting step.

a) Difference of Reactivity between the Two Heterocycles

Our choice to study in details the two model reactions has been motivated by the difference of reactivity between 4-methylpyrimidine (**1**) and methylpyrazine (**2**) towards *p*-anisaldehyde, the former being much more reactive under our experimental conditions. Indeed, if the conjugated system (**4**) (see Fig. **2**) can easily be prepared with an almost quantitative yield after only 10 minutes of reaction between **1** and **3** in a boiling aqueous solution of NaOH 5M and in the presence of 10 % mol of tetrabutylammonium hydrogen sulfate (TBAHS) (the most effective catalyst among those we previously tested [17]), the synthesis of **5** with a lower yield of 47 % requires 4 hours of reaction between **2** and **3** under the same experimental conditions. These yields have been determined by UV-visible spectroscopy (see experimental part).

As shown in the overall mechanism of this type of reactions (see Fig. **2**), the initial step consists in the formation of a carbanion from the methyldiazine, a mechanism that is favoured by an efficient delocalization of the negative charge on both atoms of nitrogen of the pyrimidine ring for **1** [19]. In case of methylpyrazine, the delocalization involves one nitrogen atom only and this heterocycle is consequently less reactive than 4-methylpyrimidine towards aromatic aldehydes. The main result of the lower reactivity of **2** is the formation of by-products arising from a Cannizzaro side-reaction [17,20]. The presence of this competitive reaction led us to use for the two model reactions, *p*-anisaldehyde, an aromatic aldehyde undergoing relatively slowly the Cannizzaro reaction.

b) Reaction between 4-methylpyrimidine and p-Anisaldehyde

If the preparation of the conjugated system (**4**) is very easy under the experimental conditions described above, it is also possible to isolate the intermediate aldol (**6**) (see Fig. **3**). This compound can be prepared with a yield of 75 % by leading, during one hour at room temperature, the reaction between 4-methylpyrimidine and *p*-anisaldehyde in an aqueous solution of NaOH 12.5M and in the presence of 2 %

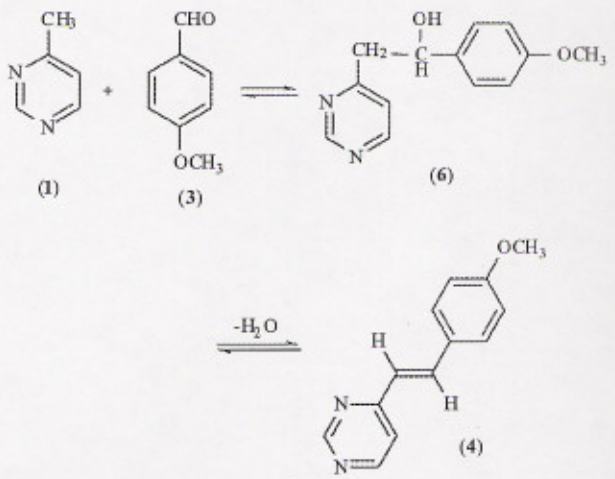


Fig. (3).

mol of cetyltrimethylammonium bromide (CTAB). The possibility to isolate this intermediate led us to suggest that the dehydration of the aldol should be the rate-limiting step of the reaction.

Table 1. Quantities of *p*-Anisaldehyde (3), Aldol (6) and Dehydrated Product (4) Present, for a given Stirring Time, in the Reaction Mixture. These Data have been Recorded by HPLC Starting from 4-methylpyrimidine and 3 (Columns 2 – 4) or from 6 (columns 5 – 7)

Time (h)	(3) (%)	(6) (%)	(4) (%)	(3) (%)	(6) (%)	(4) (%)
0	100	0	0	0	100	0
0.5	78	12	10	76	12	12
1	69	13	18	71	10	19
2	61	12	27	64	10	26
4	44	9	47	46	8	46
8	23	6	71	27	2	71
16	8	3	89	6	2	92

This proposition has been verified by comparison between the kinetic curves of formation of **4** (at 20 °C in NaOH 5 M in presence of 10 % in TBAHS) recorded either from reagents (*1*) and (*3*) or directly from the isolated aldol (under the same experimental conditions). These curves have been recorded by measuring the yields in **4** by HPLC (see Experimental part) for a given stirring time (Table **1**). As shown in Fig. (**4**), the two curves perfectly fit each other, which confirms that the dehydration reaction is the rate-limiting step ($k_4 << k_1, k_2, k_3$).

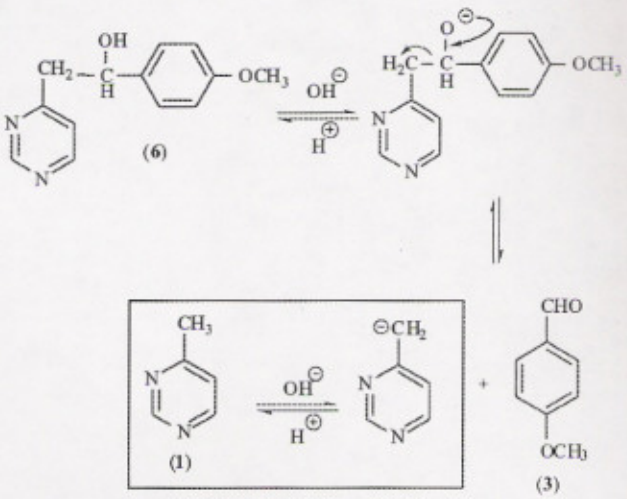


Fig. (5).

Moreover, Table 1 (column 5) reveals that *p*-anisaldehyde can easily be formed from aldol (**6**). This intermediate consequently undergoes, under the action of OH^-, a retroaldol reaction leading back to 4-methylpyrimidine and *p*-anisaldehyde (see Fig. **5**); the first three steps of this reaction are therefore equilibrated. On the other hand, the dehydration step is not reversible ($K_4 >> K_1, K_2, K_3$): no trace of aldol, 4-methylpyrimidine or *p*-anisaldehyde is detected when the dehydrated compound **4** is maintained during one hour under the experimental conditions described above.

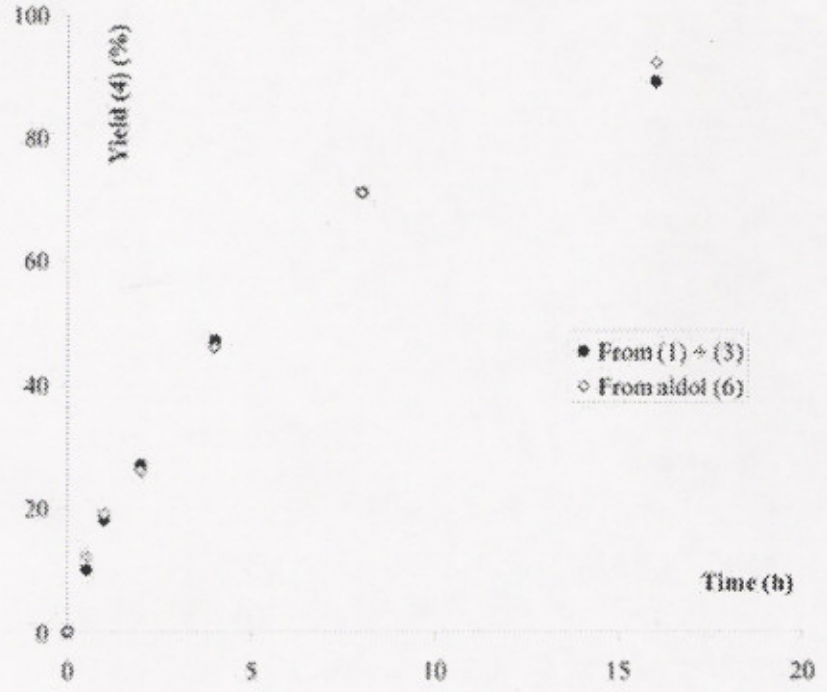


Fig. (4). Formation yield of **4** recorded either from reagents **1** and **3** or directly from the isolated aldol (**6**). Conditions: at 20 °C in NaOH 5 M in presence of 10 % in TBAHS.

c) Reaction between Methylpyrazine and p-Anisaldehyde

Contrary to the situation observed for the reaction described above, we suggest that the rate-limiting step of the reaction occurring between methylpyrazine and *p*-anisaldehyde consists in the deprotonation of the methyl group of the heterocycle ($k_1 << k_2, k_3, k_4$). No trace of aldol could indeed be detected by NMR by leading this reaction during two hours under the experimental conditions employed above at various temperatures (20, 50, 80 or 105 °C). This observation led us to assume that the intermediate aldol dehydrates as soon as it formed and that the rate-limiting step of the reaction is not the dehydration step anymore.

Moreover, the yield in dehydrated product (**5**), measured by UV-visible spectroscopy (see Experimental part), is independent of the initial concentration in *p*-anisaldehyde (only a dilution effect is observed when this concentration increases), but strongly depends on the initial concentration in methylpyrazine (Table **2**). Such results prove that only methylpyrazine acts during the rate-limiting step which should consist in the deprotonation of the methyl group of this heterocycle.

Table 2. Yield in 5 Measured (UV-Visible Spectroscopy) after 4 Hours of Stirring at 105 °C in NaOH 5M (in Presence of 10 % mol of TBAHS)

Number of equivalents in *p*-anisaldehyde	Yield in (5) (%)	Number of equivalents in methylpyrazine	Yield in (5) (%)
1	47	1	47
2	42	2	74
4	30	4	91

2. Determination of the Catalytic Activity of the Quaternary Ammonium Salt

As previously reported on [17], the presence of a quaternary ammonium salt ("quat") is necessary to reach the desired conjugated systems. Broadly speaking, the role of quats allows for favouring the contact between the hydroxide ion (from aqueous phase) and the liquid organic reagents, i.e., both the heterocycle and *p*-anisaldehyde, insoluble in the aqueous medium and constituting a "pseudo organic phase". As the hydroxide ion can act at the same time during the first (carbanion formation) and the last step (aldol dehydration) of the overall reaction mechanism and as the rate-limiting step has proven to depend upon the nature of the reacting heterocycle **1** or **2**, it has been possible to consider the role played by the catalyst either during the carbanion formation or the dehydration step by studying the reaction between, respectively, **2** and **3** or **1** and **3**.

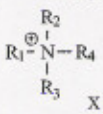
According to the literature, three catalytic processes can be invoked to take into account the catalytic activity of quats. The first process consists in an *IPTC process* [15-16] already described in the introduction. The two studied reactions could also proceed by simple phase transfer catalysis (PTC): this methodology does not necessarily require the presence of any organic solvent, the "pseudo organic phase" constituted by the liquid reagents could be sufficient [3]. It is well known [21] that the reactions led by PTC and proceed by the formation of a carbanion with an aqueous solution of NaOH (so-called PTC/OH reactions) can occur via an *interfacial* mechanism [22] or by *extraction of the hydroxide ion* into the organic phase [23].

Let's point out right away that the two condensation reactions studied in the present work occur readily without any organic solvent whereas most of the reactions proceeding by IPTC or PTC/OH require the presence of an organic solvent. Before drawing definitive conclusions, it has been preferred to discuss separately about the three possible catalytic pathways by studying the influence of the studied quats on yields in **4** and **5** (Table **3**). These yields have been determined by UV-visible spectroscopy, as discussed in the experimental part.

a) IPTC Process

Among the different quats tested for activating both studied reactions, only cetyltrimethylammonium bromide

Table 3. Yields in 4 and 5 (Determined by UV-Visible Spectroscopy) Obtained with Different Quaternary Ammonium Salts



Catalyst	R_1	R_2	R_3	R_4	X	Yield [a] (4) (%)	Yield [b] (5) (%)
none	-	-	-	-	-	1	3
a	$C_{16}H_{33}$	CH_3	CH_3	CH_3	Br	18	21
b	Ph-CH_2	C_2H_5	C_2H_5	C_2H_5	Cl	11	14
c	C_8H_{17}	C_8H_{17}	C_8H_{17}	CH_3	Cl	40	44
d	C_4H_9	C_4H_9	C_4H_9	C_4H_9	HSO_4	57	47
e	C_6H_{13}	C_6H_{13}	C_6H_{13}	C_6H_{13}	HSO_4	77	n.d.[c]
f	C_4H_9	C_4H_9	C_4H_9	C_4H_9	Cl	51	n.d.[c]
g	C_4H_9	C_4H_9	C_4H_9	C_4H_9	Br	38	n.d.[c]
h	C_4H_9	C_4H_9	C_4H_9	C_4H_9	I	14	n.d.[c]

[a] 10 min, NaOH 5 M, 50 °C, 10 % cata ; [b] 4 h, NaOH 5 M, 105 °C, 10 % cata ; [c] not determined

(CTAB – catalyst a in Table **3**) is known for forming micelles in aqueous medium. As the concentration in CTAB is 20mM while its CMC is reported at 1 mM [24], this quat could thus be *a priori* proceed in this way.

Whereas, for the condensation reaction led in NaOH 0.25 M between acetophenone and benzaldehyde, the formation of the chalcone is less efficient in the presence of quats unable to form micelles (e.g. tetrabutylammonium chloride or tetrabutylammonium hydroxide) as compared to CTAB [9], it appears that, in our case, the catalytic activity of CTAB is reduced compared to Aliquat®336 (catalyst c) and tetrabutylammonium hydrogen sulfate (TBAHS – catalyst d). Therefore, one cannot exclude that CTAB proceeds, in spite of micelles formation, by PTC rather than by IPTC *(vide infra)*.

The catalytic activity of Aliquat®336 could also be attributed to an IPTC process as this quat forms small aggregates (not micellar) [25] but a PTC/OH process may not be excluded again. As benzyltriethylammonium chloride (TEBACl – catalyst b) and TBAHS are unable to form micelles (in view of their limited size), they must necessarily proceed by PTC/OH and not by IPTC.

b) PCT/OH Process (Interfacial)

When this process occurs, the carbanion is formed at the interface between aqueous and organic phases and the role of the quat consists in to displace this carbanion away from the interface (as an ion pair); the reaction occurring actually in the organic phase. To be correctly efficient, quats have to display a positive charge relatively well accessible [21] but also can reduce significantly the surface tension between aqueous and organic phases [26]. Typically, quats possessing short alkyl chains as TEBACl are the most frequently reported ammonium salts in PTC/OH interfacial process.

It appears that among the four tested catalysts, TEBACl is the less efficient whereas the highest activity is displayed by TBAHS (see Table **3**). Considering that the positive charge in TBAHS is less accessible than in TEBACl, it seems unlikely that the catalytic activity of these quats could be attributed to a PTC/OH interfacial process.

Interestingly enough, two other arguments hold to rule out this interfacial process. First, the conversion in **4** and **5** is almost non-existent in the absence of quat, whereas, Makosza demonstrated the importance of that process by leading successfully the alkylation of phenylacetonitrile without catalyst [27]. Next, the yields in **4** and **5** do not seem to depend on the stirring rate imposed on the reaction medium, all the other conditions kept unchanged (see Table **4**), whereas, it has been reported that the kinetic of a reaction proceeding by an interfacial mechanism directly depends on the stirring rate [28].

Table 4. Yields in 4 and 5 *Versus* Stirring Rate (in rpm)

Stirring rate (rpm)	Yield [a] (4) (%)	Yield [b] (5) (%)
500	53	48
1000	57	47

[a] 10 min, NaOH 5 M, 50 °C, 10 % TBAHS ; [b] 4 h, NaOH 5 M, 105 °C, 10 % TBAHS

c) PTC/OH Process (Hydroxide Ion Extraction)

This process is characterized by the extraction of the hydroxide ion from the aqueous phase into the organic phase; the carbanion is thus formed in the latter and the condensation reaction occurs also into that phase.

Considering that the catalytic activity of TBAHS and TEBACl cannot reasonably explained either by IPTC or by a PTC/OH interfacial process; a PTC/OH extraction process has been invoked. Indeed, three major arguments support this hypothesis.

First, as shown above, the yields in **4** and **5** are, in the presence of TBAHS, independent of the stirring rate imposed to the reaction medium. Such behaviour is typical of reactions proceeding by PTC/OH extraction; many authors have obtained similar results [21, 29-31]. Halpern *et al.* showed, by studying the isomerization reaction of allylbenzene that this behaviour could be explained by the fact that the ion pair Q^+OH^- quickly reaches a stable concentration in the organic phase [32]: under a given stirring rate (300 rpm under the experimental conditions used in [32]) the reaction kinetics, controlled by diffusion phenomena, depend on the stirring rate whereas, above this limit stirring rate, a stable concentration in Q^+OH^- is reached and the reaction does not depend on the stirring rate anymore.

A second argument relies upon the molecular structure of the studied quats. Dehmlow *et al.* showed that the efficiency of the hydroxide ion extraction increases with the lipophilicity of the quaternary ammonium cation and that the use of quats possessing long alkyl chains is particularly favourable for reactions proceeding by PTC/OH extraction [33]. Although the two studied condensation reactions occur without organic solvent, it appears that the experimental results described in Table 3 remarkably correlate to the observations by Dehmlow *et al.*. Among the four catalysts tested, the most efficient are Aliquat®336 (c) and TBAHS (d); they possess both longer alkyl chains than CTAB (a) and TEBACl (b) and can shuttle OH^- more efficiently in the organic phase. Thus, even if an IPTC process is possible to explain the catalytic activity of (a) and (c), this PTC mechanism is also realist. This proposition has been confirmed by the use of more lipophilic quat (e), formed of four hexyl chains in place of four butyl chains for (d), which leads to an increase of the yield in **4**, as expected for the proposed PTC process.

Finally, it is also known that the efficiency of reactions proceeding by this mechanism strongly depends on the counter-ion associated to Q^+: the hydroxide ion is indeed a hard base and associates with difficulty with soft cations as Q^+, especially in the presence of soft counter-ions as bromide or iodide anions [21]. For the reaction between 4-methylpyrimidine and *p*-anisaldehyde, the yields in **4** have been determined in the presence of different tetrabutylammonium salts (see Table **3**, catalysts (d), (f), (g) and (h)) and it appears that reducing the softness of the anions triggers an increase of the yield in **4**: it falls to 14 % if the counter-ion consists in iodide anion, the softest of the four anions considered. These complementary results seem to fully confirm the occurrence of this third PTC/OH extraction process.

CONCLUSIONS

Two model reactions have been studied: first, to determine the reaction scheme of aldol condensations of (di)methyldiazines and aromatic aldehydes led in aqueous medium (solution of NaOH) in the absence of any organic solvent, and second, to understand the catalytic action of quaternary ammonium salts ("quats") during these reactions. These model reactions concern the reactions between 4-methylpyrimidine or methylpyrazine and *p*-anisaldehyde.

The key step of such reactions is the deprotonation of the methyl group of the heterocycle. We showed that this step is faster from 4-methylpyrimidine than from methylpyrazine and, consequently, the rate-limiting step differs from the two reactions: it consists in the dehydration step of the intermediate aldol for the reaction implicating 4-methylpyrimidine and in the initial deprotonation of methylpyrazine for the other studied reaction.

Such reactions are catalyzed by quats and we propose that these catalysts act by transfer of an hydroxide ion in the "pseudo organic phase" constituted by the liquid reagents, not only during the deprotonation step but also during the dehydration step; one can speak of PTC/OH extraction process. However, an IPTC process may not be ruled out for certain catalysts as CTAB or Aliquat®336.

Experimental Part

Solvents and reagents are commercially available (Acros Organics, Aldrich Co) and were used without further purification. ^{1}H NMR spectra ($CDCl_3$) were recorded on a Bruker AMX spectrometer (300 MHz at 7.0 T). UV spectra were recorded on a Varian Cary 50 spectrophotometer. HPLC chromatograms were recorded on a Waters 600 E equipped with a U6K injector and a Waters 486 UV-detector. Compounds **4**, **5** and **6** have been described in the literature [34].

General Procedure for the Preparation of (4) and (5)

A stoichiometric mixture of methyldiazine * (5 mmol; 0.46 ml) and *p*-anisaldehyde (5 mmol; 0.61 ml) in an aqueous solution of sodium hydroxide 5 M (25 ml) containing a quaternary ammonium salt (0.5 mmol) was thermostatized at 20 or 105 °C and maintained under stirring (1000 rpm) for a given time. After cooling, the crude product was filtered off and recrystallized in petroleum ether.

*4-methylpyrimidine or Methylpyrazine

The yields in **4** and **5** were determined by UV-spectrometry and by diluting the reaction mixture with ethanol in order to adjust the final volume to 100 ml. A sample of that stock solution was then diluted 500 times with ethanol, and the UV spectrum was recorded (under similar conditions, we recorded $\varepsilon = 25000$ at $\lambda_{max} = 342$ nm for a pure sample of **4** and $\varepsilon = 21000$ at $\lambda_{max} = 347$ nm for a pure sample of **5**.

Preparation of the Intermediate Aldol (6)

A stoechiometric mixture of 4-methylpyrimidine (5 mmol; 0.46 ml) and *p*-anisaldehyde (5 mmol; 0.61 ml) in an aqueous solution of sodium hydroxide 5 M (25 ml) containing cetyltrimethylammonium bromide CTAB (0.1 mmol; 0.04 g) and thermostatized at 20°C was maintained under stirring (1000 rpm) for one hour. Then, the crude product was filtered off and recrystallised in cyclohexane.

Kinetic Study of the Aldol Condensation of 4-Methylpyrimidine on *p*-Anisaldehyde (Determination of the Rate-Limiting Step)

A stoichiometric mixture of 4-methylpyrimidine (5 mmol; 0.46 ml) and *p*-anisaldehyde (5 mmol; 0.61 ml) in an aqueous solution of sodium hydroxide 5 M (25 ml) containing TBAHS (0.5 mmol; 0.17 g) was thermostatized at 20 °C and maintained under stirring (1000 rpm) for 0.5, 1, 2, 4, 8 or 16 hours. Then, the reaction mixture was extracted with dichloromethane (3 X 25 ml). The solution was dried on magnesium sulfate, and the solvent was removed by evaporation under reduced pressure. The composition of the residue in **3**, **4** and **6** has been determined by HPLC: the mobile phase was constituted by a mixture of methanol and water (1: 1) with a flow rate of 1 ml/min; the stationary phase consisted in a Novapak C18 column; the UV detection occurred at a wavelength of 228 nm; and the retention times were 2.5, 3.5 and 14 minutes (respectively for (**6**), (**3**) and (**4**)).

A totally similar procedure has been employed to study the dehydration of the aldol (**6**): in that case, **6** (5 mmol; 1.15 g) or **4** (5 mmol; 1.06 g) was used in place of 4-methylpyrimidine and *p*-anisaldehyde.

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REFERENCES

[1] House, H.O. *Modern Synthetic Reactions, 2nd Ed.*, Benjamin, W.A., Inc. Menlo Park, California, **1972**.
[2] March, J. Advanced Organic Chemistry, 4th Ed., Wiley, **1992**.
[3] Dehmlow, E.; Dehmlow, S.S. *Phase Transfer Catalysis, 2nd Ed.*, VCH: Weinheim, **1983**.
[4] Li, C.J. *Chem. Rev.*, **1993**, *93*, 2023.
[5] Lubineau, A.; Augé, J.; Queneau, J. *Synthesis*, **1994**, 741.
[6] Lubineau, A.; Augé, J. In *Topics in Current Chemistry*, Springer-Verlag: Berlin Heidelberg, **1999**; Vol. *106*.
[7] Engberts, J.B.F.N.; Feringa, B.; Keller, E.; Sijbren, O. *Recl. Trav. Chim. Pays-Bas*, **1996**, *115*, 457.
[8] Nivalkar, K.R.; Mudaliar, C.D.; Mashraqui, S.H. *J. Chem. Research (S)*, **1992**, 98.
[9] Fringuelli, F.; Pani, G.; Piermatti, O.; Pizzo, F. *Tetrahedron*, **1994**, *50*, 11499.
[10] Vanden Eynde, J.J.; Mutonkole, K.; Van Haverbeke, Y. *Ultrasonics Sonochemistry*, **2001**, *8*, 35.
[11] Brufola, G.; Fringuelli, F.; Piermatti, O.; Pizzo, F. *Heterocycles*, **1997**, *45* (9), 1715.
[12] Ballini, R.; Bosica, G. *Tetrahedron Lett.*, **1996**, *37* (44), 8027.
[13] Mudaliar, C.D.; Nivalkar, K.R.; Mashraqui, S.H. *OPPI BRIEFS*, **1997**, *29* (5), 584.
[14] Ballini, R.; Bosica, G. *Eur. J. Org. Chem.*, **1998**, 355.
[15] Boyer, B.; Betzer, J.F.; Lamaty, G.; Leydet, A.; Roque, J.P. *New J. Chem.*, **1995**, *19*, 807.
[16] Boyer, B.; Hambardzoumian, A.; Roque, J.P.; Beylerian, N. *Tetrahedron*, **2000**, *56*, 303.

[17] Vanden Eynde, J.J.; Pascal, L.; Van Haverbeke, Y.; Dubois, P. *Synth. Commun.*, **2001**, *31* (20), 3167.
[18] Pascal, L.; Vanden Eynde, J.J., Van Haverbeke, Y., Dubois, P.; Michel, A.; Rant, U.; Zojer, E.; Leising, G.; Van Dorn, L.O.; Gruhn, N.E.; Cornil, J.; Brédas, J.L. *J. Phys. Chem. B*, **2002**, *106*, 6442.
[19] Batterham, J.J.; Brown, D.J.; Paddon-Row, M.N. *J. Chem. Soc. B*, **1967**, 171.
[20] Geissman, T.A. *Org. Reactions*, **1944**, *2*, 94.
[21] Rabinovitz, M.; Cohen, Y.; Halpern, M. *Angew. Chem. Int. Ed. Engl.*, **1986**, *25*, 960.
[22] Makosza, M. *Pure Appl. Chem.*, **1975**, *43*, 439.
[23] Starks, C.M. *J. Am. Chem. Soc.*, **1971**, *93*, 195.
[24] Dam, T.; Engberts, J.B.F.N.; Karthaüser, J.; Karaborni, S.; Van Os, N.M. *Colloids Surf. A*, **1996**, *118*, 41.
[25] Bunton, C.A.; Savelli, G. *Adv. Phys. Org. Chem.*, **1986**, *22*, 214.
[26] Mason, D.; Magdassi, S.; Sasson, Y. *J. Org. Chem.*, **1990**, *55*, 2714.
[27] Makosza, M.; Bialecka, E. *Tetrahedron Lett.*, **1977**, 183.
[28] Menger, F.; *J. Am. Chem. Soc.*, **1970**, 5965.
[29] Herriott, A.W.; Picker, D. *Tetrahedron Lett.*, **1972**, 4521.
[30] Starks, C.M.; Owens, R. *J. Am. Chem. Soc.*, **1973**, *95*, 3613.
[31] Landini, D.; Maia, A.; Montenari, F. *J. Am. Chem. Soc.*, **1978**, *100*, 2796.
[32] Halpern, M.; Sasson, Y.; Rabinovitz, M. *J. Org. Chem.*, **1983**, *48*, 1022.
[33] Dehmlow, E.; Slopianka, M.; Heider, J. *Tetrahedron Lett.*, **1977**, 2361.
[34] Haroutounian, S.; Katzenellenbogen, J. *Tetrahedron*, **1995**, *51* (6), 1585.