Mono-N-methylation of Primary Amines with Alkyl Methyl Carbonates over Y Faujasites. 2. Kinetics and Selectivity

Maurizio Selva,* Pietro Tundo, and Alvise Perosa

Dipartimento di Scienze Ambientali dell'Università Ca' Foscari, Calle Larga S. Marta 2137, 30123 Venezia, Italy
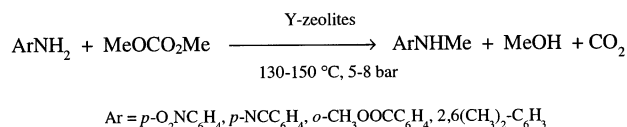
selva@unive.it

In the presence of a Na-exchanged Y faujasite, the reaction of primary aromatic amines **1** with 2-(2-methoxyethoxy)methylethyl carbonate [$MeO(CH_2)_2O(CH_2)_2OCO_2Me$, **2a**] yields the corresponding mono-*N*-methyl derivatives ArNHMe with selectivity up to 95%, at substantially quantitative conversions. At 130 °C, the reaction can be run under diffusion-free conditions and is strongly affected by the solvent polarity: for instance, in going from xylene ($\epsilon_r = 2.40$) to triglyme ($\epsilon_r = 7.62$) as the solvent, the pseudo-first-order rate constant for the aniline (**1a**) disappearance shows a 5-fold decrease. In DMF ($\epsilon_r = 38.25$), the same reaction does not occur at all. Competitive adsorption of the solvent and the substrate onto the catalytic sites accounts for this result. The behavior of alkyl-substituted anilines $ZC_6H_4NH_2$ [Z = *p*-Me, *p*-Et, *p*-Pr, *p*-(*n*-Bu) (**1b**−**e**); Z = 3,5-di-*tert*-butyl- and 2,4,6-tri-*tert*-butylanilines (**1f,g**)] and *p*-alkoxyanilines *p*-$ZC_6H_4NH_2$ [Z = OMe, OEt, OPr, O-*n*-Bu (**1b′**−**e′**)] clearly indicates a steric effect of ring substituents: as diffusion of the amine into the catalytic pores is hindered, the reaction hardly proceeds and the mono-*N*-methyl selectivity ($S_{M/D}$) drops as well. Moreover, the strength of adsorption of the amine onto the catalyst influences the rate and the selectivity as well: the reaction of *p*-anisidine and *p*-toluidine—despite the higher nucleophilicity of these compounds—is slower and even less selective with respect to aniline. From a mechanistic viewpoint, the intermediacy of carbamates $ArN(Me)CO_2R$ [R = $MeO(CH_2)_2O(CH_2)_2$] is suggested. At 90 °C, the reaction of benzylamine (**7**)—a model for aliphatic amines—with dimethyl carbonate shows that the reaction outcome can be improved by tuning the amphoteric properties of the catalyst: in going from CsY to the more acidic LiY zeolite, methylation is not only more selective ($S_{M/D}$ ratio increases from 77% to 84%) but even much faster (CsY, conversion of 36% after 22 h; LiY, conversion of 43% after 7 h).

Introduction

The direct mono-N-alkylation of primary amines is not usually performed with conventional alkylation procedures because competing overalkylation reactions lead to mixtures of secondary and tertiary amines along with the corresponding ammonium salts.[1] This is particularly the case for N-methylation reactions.

A few years ago, we reported that a very high mono-*N*-methyl selectivity can be attained when primary aromatic amines **1** are allowed to react with dimethyl carbonate (DMC) as the alkylating agent in the presence of alkali-metal-cation-exchanged faujasites as the catalysts (Scheme 1).[2] Typically, at 120−150 °C (*P* = 2−6 bar[3]), the formation of *N*-methylanilines **3**—even deactivated ones (XC_6H_4NHMe, X = *p*-O_2N, *p*-CN, *o*-MeO_2C)—

SCHEME 1

$$ArNH_2 + MeOCO_2Me \xrightarrow[\text{130-150 °C, 5-8 bar}]{\text{Y-zeolites}} ArNHMe + MeOH + CO_2$$

Ar = *p*-$O_2NC_6H_4$, *p*-NCC_6H_4, *o*-$CH_3OOCC_6H_4$, 2,6(CH_3)$_2$-C_6H_3

takes place with a selectivity of 92−98%, at conversions of 72−93%.

More recently, we demonstrated that this alkylation procedure is a general one:[4] anilines react with different dialkyl carbonates **2** to yield the corresponding mono-N-alkylated derivatives XC_6H_4NHR (X = H, Cl, NO_2; R = Me, Et, Bn, allyl) with a selectivity of 90−97% in good to excellent yield (68−94%). It was also observed that the reaction can be conveniently carried out at atmospheric pressure with the use of high-boiling-point unsymmetrical dialkyl carbonates $ROCO_2R′$ [R = Me, Et; R′ = $MeO(CH_2)_2O(CH_2)_2$ (**2b** and **2c**, respectively)]:[5] a chemoselectivity of up to 99% toward N-methylation and N-ethylation was achieved (Scheme 2).

---

* To whom correspondence should be addressed. Fax: +39 041 234 8620.

(1) (a) Gibson, M. S. In *The Chemistry of Amino Groups*; Patai, S., Ed.; Interscience Publishers: London, 1968. (b) March, J. In *Advanced Organic Chemistry*, 4th ed.; Wiley: New York, 1991.

(2) Selva, M.; Bomben, A.; Tundo, P. *J. Chem. Soc., Perkin Trans. 1* **1997**, 1041.

(3) Reactions must be run in sealed vessels (autoclaves) at temperatures over the boiling point of DMC (90 °C).

(4) Selva, M.; Tundo, P.; Perosa, A. *J. Org. Chem.* **2001**, *66*, 677.

(5) Perosa, A.; Selva, M.; Tundo, P., Zordan, F. *Synlett* **2000**, *1*, 272−274.

SCHEME 2

$$ArNH_2 + ROCO_2R' \xrightarrow[130\text{-}160\ ^\circ C,\ 1\ atm]{NaY} ArNHR + ROH + CO_2$$

R = Me, Et; R' = MeO(CH$_2$)$_2$O(CH$_2$)$_2$; Ar = Ph, *p*-O$_2$NC$_6$H$_4$, *p*-Cl

The environmentally benign features of these reactions should also be noted: organic carbonates are much more ecocompatible than conventional alkylating agents (i.e., alkyl halides or dialkyl sulfates),[6] and they produce neither organic nor inorganic wastes to be disposed of.[7]

The novelty and the good performance of this procedure prompted us to undertake a more detailed investigation of the features of these reactions and, most of all, of the factors affecting selectivity. In this paper, we report some of the general conclusions drawn from the analysis of the kinetics of the mono-methylation reaction of different primary amines carried out in the presence of several Y-type zeolites.

Results and Discussion

Mono-N-methylation of Aniline. (i) Experimental Conditions. As aforementioned, selective mono-N-methylations of anilines can be achieved at atmospheric pressure with the use of unsymmetrical methyl alkyl carbonates ROCO$_2$Me. This is advantageous (with respect to DMC) for the setup of a kinetic investigation because reactions can be monitored more easily in conventional glass reactors.

Accordingly, the mono-N-methylation of aniline (**1a**) with 2-(2-methoxyethoxy)ethyl methyl carbonate [MeO-(CH$_2$)$_2$O(CH$_2$)$_2$OCO$_2$Me, **2a**] was investigated as a model reaction (eq 1).

$$\underset{\textbf{1a}}{PhNH_2} + \underset{\textbf{2a}}{ROCO_2Me} \xrightarrow{NaY} PhNHMe + ROH + CO_2$$

(1)

$$R = MeO(CH_2)_2O(CH_2)_2$$

Initial experiments were carried out using solutions (0.45 M, 5 mL) of **1a** in triglyme [MeO(CH$_2$CH$_2$O)$_3$Me] which were made to react at 130 °C (atmospheric pressure) with different amounts of **2a** [molar ratio **2a**:**1a** (*W*) in the range of 2–6] in the presence of the faujasite NaY as the catalyst [weight ratio (*Q*) NaY:**1a** = 0.5].[8] The conversion of aniline was monitored by GLC over a period of 8 h for each run.

Figure 1 reports the results.

As the *W* ratio increases from 2 to 4, the conversion rises as well from 40% to 80%. Then, further increments in the quantity of **2a** (*W* ≥ 4) do not have any appreciable effect on the reaction conversion, which is substantially unaltered (∼80%). This may indicate that, at *W* ≥ 4, the concentration of the carbonate adsorbed by the zeolite

FIGURE 1. Mono-N-methylation of aniline with **2a** at 130 °C: reaction conversions after 8 h.

reaches the maximum allowed value and remains constant throughout the reaction.

In all cases reported in Figure 1, the mono-*N*-methyl selectivity is 99%.

(ii) Order and Regime of Reaction. Under the conditions of point i, reaction 1 was run using a *W* ratio of 5, and with the addition of *n*-tetradecane as the internal standard.

Figure 2a reports both the disappearance of aniline and the formation of its *N*-methyl derivative. At a high conversion (>70%), the mass balance falls within a 5% range because of the concurrent formation of PhN(R)Me [R = MeO(CH$_2$)$_2$O(CH$_2$)$_2$, ≤1%, by GC] along with a nonidentified byproduct (≤4%).

If one considers that the concentration of the carbonate **2a** adsorbed by the zeolite is a constant during the reaction,[9] a simplified rate law equation can be used (eq 2, where $K' = k[\textbf{2a}]^q$).

$$v = -\left(\frac{d[\textbf{1a}]}{dt}\right) = k[\textbf{1a}]^p[\textbf{2a}]^q = K'[\textbf{1a}]^p \qquad (2)$$

Apparently, the decay of aniline follows a first-order rate law (Figure 2a). This is confirmed by Figure 2b, which shows that the concentration of aniline (determined by GC) fits the integrated expression of eq 2 with $p = 1$ well, i.e., $\ln([\textbf{1a}]_0/[\textbf{1a}]) = K't$ ([**1a**]$_0$ and [**1a**] = concentrations of **1a** at $t = 0$ and at a later time t, respectively). The resulting plot gives a straight line ($r > 0.99$) whose slope is the pseudo-first-order rate constant k_{obs} for the disappearance of the substrate ($k_{obs} = 4.9 \times 10^{-3}$ min^{-1}).

However, before the discussion of any kinetic result, it was compulsory to establish the regime under which reaction 1 occurred: in fact, especially zeolite-catalyzed processes (where the inner cages of the catalyst have sizes comparable to the those of the reactant molecules) could be seriously limited by diffusion phenomena.[10] To this scope, the formal treatment for heterogeneous catalytic reactions was applied:[11] i.e., the effect of both the catalyst weight and the stirring rate on the kinetic constant (k_{obs} in eq 2), as well as the activation energy of

(6) Romano, U.; Rivetti, F.; Delledonne, D. In *Green Chemistry, Designing Chemistry for the Environment*; Anastas, P. T., Williamson, T., Eds.; ACS Symposium Series 626; American Chemical Society: Washington, DC, 1996.

(7) The coproduct alcohol ROH (Scheme 2) can in principle, be recycled to the preparation of the carbonate itself.

(8) Initial reaction conditions were chosen on the basis of results already reported by our group (see ref 4).

(9) According to Figure 1, this assumption holds on the condition that the *W* ratio be ≥4. Hence, eq 2 can be applied for the results of Figure 2 (*W* = 5).
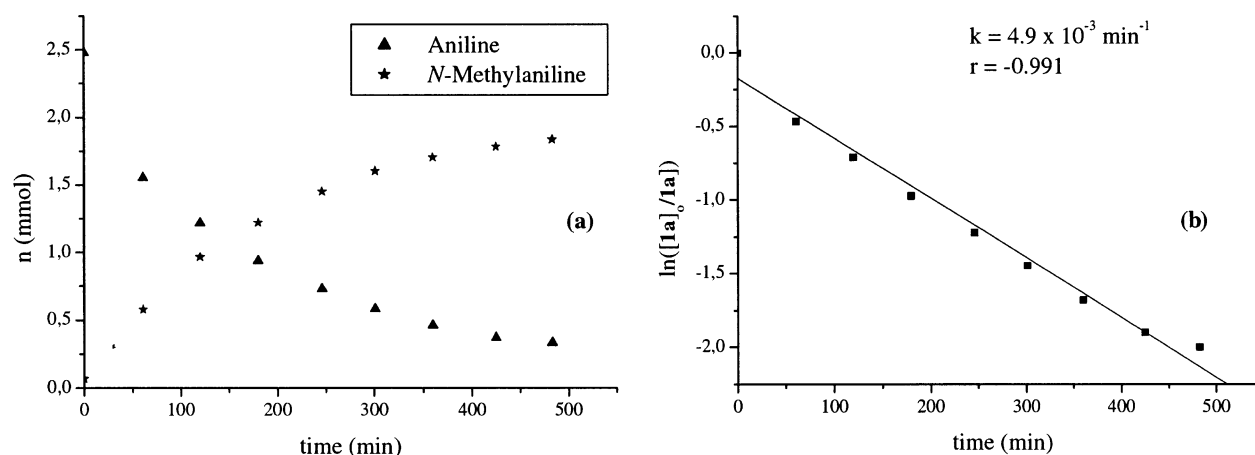
FIGURE 2. Mono-N-methylation of aniline with carbonate **2a** at 130 °C ($W = 5$): disappearance of aniline (▲) and formation of N-methylaniline (*) (a); pseudo-first-order rate constant plot for aniline (b).
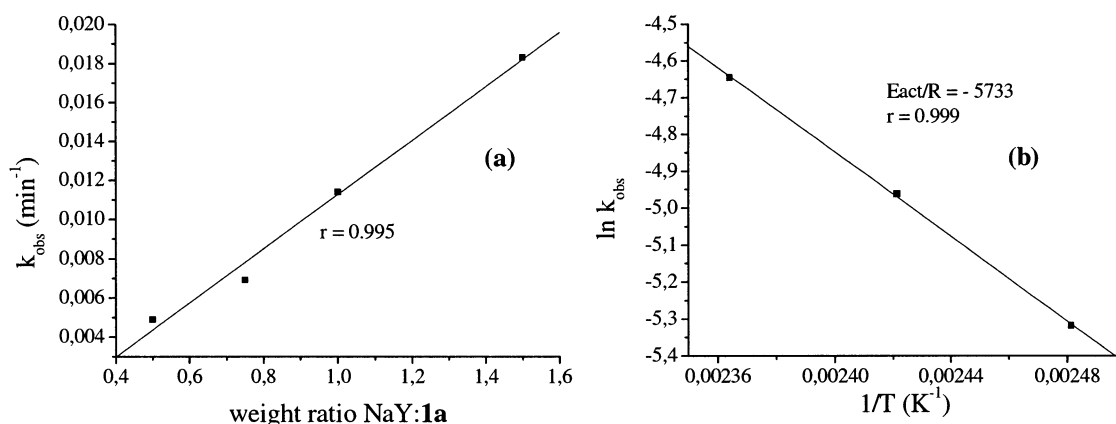

FIGURE 3. (a) Pseudo-first-order rate constants for the disappearance of aniline as a function of the catalyst weight. (b) Arrhenius plot of reaction 1 in the range of 130−150 °C.

reaction 1, were investigated.[12] Under the conditions of Figure 2 ($T = 130$ °C, $W = 5$), two sets of experiments (I and II) were carried out: reaction 1 was run (a) by varying the Q ratio (weight ratio NaY:**1a**) in the range of 0.5−1.5 and (b) at a Q of 0.5, with different stirring rates of 600 and 1000 rpm. The constant k_{obs} was determined in all cases, and each reaction was repeated twice to check the reproducibility.

In the first set (I), it was found that k_{obs} increased linearly with the catalyst amount (Figure 3a),[13] while set II showed that k_{obs} was substantially independent of the stirring rate ($k_{obs} = 5.0 \times 10^{-3}$ and 4.9×10^{-3} min^{-1} at 600 and 1000 rpm, respectively).

Moreover, under the conditions of Figure 2 ($W = 5$, $Q = 0.5$), reaction 1 was investigated in the range of temperature from 130 to 150 °C, and an activation energy of 48 kJ mol^{-1} was calculated from the corresponding Arrhenius plot (ln $k_{obs} =$ ln $A - E_{att}/RT$; Figure 3b). This value was well above the threshold of 25 kJ mol^{-1} accepted for chemically controlled reactions.[14]

To summarize, the data of Figure 3 as well as the effect of the stirring on the reaction rate allowed the conclusion that reaction 1 was not diffusion controlled under the examined conditions.[15] Hence, the kinetic treatment could be validated.

(iii) Effect of the Solvent. To investigate the influence of the solvent polarity, the mono-N-methylation of aniline with **2a** was carried out in the presence of aprotic reaction media having dielectric constants either higher or lower with respect to that of triglyme ($\epsilon_r = 7.62$): in

(10) (a) Thomas, J. M.; Thomas, W. J. *Principle and Practice of Heterogeneous Catalysis*; VCH: Veinheim, 1997; Chapter 4. (b) Carberry, J. J. In *Catalysis: Science and Technology*; Andersen, J. R., Boudart, M., Eds.; Springer-Verlag: Berlin, 1987; Vol. 8, Chapter 3. (c) Eberly, P. E. In *Zeolite Chemistry and Catalysis*; Rabo, J. A., Ed.; ACS Monograph 171; American Chemical Society: Washington, DC, 1976; Chapter 7.

(11) Reyes, S. C.; Iglesia, E. *J. Catal.* **1991**, *129*, 457

(12) As reported by Simpson et al.,[12a] the most appropriate analysis of this effect for zeolites is the approach of Weisz−Prater.[12b] This model, however, was not applicable for reaction 1 because the diffusional coefficients (D) of the reactants were not available. (a) Simpson, M. F.; Wei, J.; Sundaresan, S. *Ind. Eng. Chem. Res.* **1996**, *35*, 3861. (b) Weisz, P. B.; Prater, C. D. *Adv. Catal.* **1954**, *6*, 143.

(13) Values of k_{obs} are averaged over two runs: at any given Q, the two k_{obs} values were within a maximum of a 10% deviance from each other.

(14) Bond, G. C. *Heterogeneous catalysis principles and applications*, 2nd ed.; Clarendon Press: Oxford, 1987.

(15) This procedure was also applied to demonstrate the absence of diffusional effects for several reported zeolite-catalyzed reactions, i.e., the N-methylation of melamine catalyzed by Ru mordenites,[15a] the *trans*-alkylation of diethylbenzene/benzene in the presence of H faujasites,[15b] and the oligomerization of isobutene with H mordenites.[15c] (a) Shinoda, S.; Fujimura, K.; Ohnishi, T.; Yamakawa, T. *Appl. Catal., A* **2000**, *194−195*, 375. (b) Tiako Ngandjui, L. M.; Louhibi, D.; Thyrion, F. C. *Chem. Eng. Process.* **1997**, *36*, 133. (c) Tiako Ngandjui, L. M.; Thyrion, F. C. *Chem. Eng. Process.* **1992**, *31*, 1

TABLE 1. Influence of the Solvent Polarity in the N-Methylation of Aniline with 2a

	solvent	ϵ_r	$k_{obs} \times 10^{-2\,a}$ (min^{-1})	convn (%)	$S_{M/D}{}^e$ (%)	3a yield^f (%, GC)
1	xylene	2.40	2.29	98	99	92
2	triglyme	7.62	0.49	85	99	82
3	triglyme with nondried NaY	7.62	0.42	79	99	75
4	DMF	38.25	na^b	3	99	3
5	c	6.14^d	2.41	100	99	94

^{a} k_{obs} values are averaged over two reactions carried out for each solvent. ^{b} na = not available. ^{c} The reaction was run with only the carbonate **2a** in a 5-fold molar excess with respect to aniline. No additional solvent was used. ^{d} The dielectric constant of **2a** was determined as reported in the Experimental Section. ^{e} $S_{M/D}$ = mono-*N*-methyl selectivity defined as [PhNH(CH$_3$)]/([PhNH(CH$_3$)] + [PhN(CH$_3$)$_2$]) × 100. ^{f} Yield of **3a** (*N*-methylaniline) determined by GC.

particular, *N,N*-dimethylformamide (DMF, ϵ_r = 38.25) and xylene (ϵ_r = 2.40) were employed.[16] Experiments were run under the conditions previously reported (130 °C, *Q* = 0.5, and *W* = 5), and in all cases, solutions (0.4 M, 5 mL) of aniline in the given solvent were used. *n*-Tetradecane and ethylene glycol di-*n*-hexyl ether (*n*-C$_6$H$_{13}$OCH$_2$CH$_2$O-*n*-C$_6$H$_{13}$) were the internal standards for reactions with xylene and DMF, respectively. Reaction 1 was also performed in the presence of only the carbonate **2a** with no additional solvent.

As described above (point ii), pseudo-first-order rate constants (k_{obs}) were evaluated for the disappearance of aniline. The results are reported in Table 1.

The data clearly show that although the reaction selectivity is not affected by solvent polarity, the nature of the solvent has a dramatic effect on the reaction rate. As the dielectric constant increases, k_{obs} markedly drops (entries 1−3), to the point that it is no more determinable in the more polar medium (DMF) where the reaction is inhibited (after 8 h, conversion was 3%, entry 4). By contrast, the fastest reaction takes place when no additional solvents are used (entry 5).

The rationale for this behavior can be found in the large difference in the strength of adsorption between polar and apolar solvents onto the zeolite. Polar compounds such as DMF interact strongly with the polar environment (i.e., a silicoaluminate structure) of the inner cages of the faujasite, while the apolar xylene is hardly retained. Consequently, the polar solvent itself becomes the major competitor of aniline for the active sites of the catalyst, and the corresponding reaction rate falls.

This explanation may also account for the outcome in the absence of added solvents (entry 5): the higher rate constant is due to a 2-fold effect of the relatively low polarity of **2a** (ϵ_r = 6.14), and of the lack of competitive phenomena of adsorption.

However, regardless of the solvent used, the reaction proceeds toward the formation of only mono-*N*-methylaniline: once the reactant amine is adsorbed, the very high selectivity is induced by the structure/polarity features of the catalyst.

Similar effects have also been described for the cyclo-

(16) *CRC Handbook of Chemistry and Physics*, 75th ed.; Lide, D. R., Ed.; CRC Press: Boca Raton, FL, 1994.

TABLE 2. Reaction of 1a, 1b, and 1b′ with 2a at 130 °C in the Presence of NaY

entry	amine	*x* (Å)	*y* (Å)	*z* (Å)	NaY:1^a (g/g)	solvent	*t* (h)	convn (%)	$S_{M/D}{}^b$ (%)	$k_{obs} \times 10^{-2}$ (min^{-1})
1	**1a**	4.34	1.17	5.59	0.5	xylene	3	98	99	2.29
2	**1b**	4.34	1.81	6.44	0.5	xylene	7	66	94	0.24
3	**1b′**	4.60	1.86	7.89	0.5	xylene	7	56	85	0.17
4	**1b′**				1	xylene	7	86	81	3.8
5	**1b′**				0.5	triglyme	7	18	94	na^c
6	**1b′**				1	triglyme	7	51	93	1.6
7	**1b′**				1	triglyme	16	76	88	na

^{a} Weight ratio between the catalyst NaY and the amine **1**. ^{b} $S_{M/D}$ defined as in Table 1. ^{c} Not available.

hexylation of phenol over USHY faujasites,[17] and for the Fries rearrangement of phenyl acetate over HBEA zeolites:[18] in both cases, the authors claimed that reaction rates were strongly depressed in the presence of polar solvents able to adsorb onto the acidic sites of the catalysts.

Finally, it should be noted that only a modest decrease of the catalytic activity is observed when the reaction is carried out with a faujasite not preliminarily dried (compare entries 2 and 3): the amount of water (5−7 wt %) adsorbed by the catalyst may account for this result.[19]

Mono-N-methylation of *p*-Alkyl- and *p*-Alkoxy-Substituted Anilines. Our previous results suggested that the adsorption of anilines and dialkyl carbonates onto the cages of Y zeolites, and consequently the selectivity of the mono-N-alkylation reactions, could be controlled by the pore size and amphoteric properties of the catalysts.[2,4] To understand this phenomenon, a comparative study on a homologous series of anilines was undertaken. In particular, *p*-alkyl- and *p*-alkoxyanilines *p*-ZC$_6$H$_4$NH$_2$ [Z = Me, Et, Pr, *n*-Bu (**1b−e**); Z = OMe, OEt, OPr, O-*n*-Bu (**1b′-e′**)] appeared to be appropriate substrates to describe the influence of both the bulkiness and the electronic properties of the substituents.

***p*-Toluidine and *p*-Anisidine**. At first, the reactivities of the lightest terms of the two series, *p*-toluidine (**1b**) and *p*-anisidine (**1b′**), were compared. At 130 °C, solutions (5 mL, 0.3 M) of these amines in xylene or triglyme as the solvent were made to react with the carbonate **2a** (in a 5-fold molar excess with respect to the amine) and the zeolite NaY. *n*-Dodecane (in xylene) and diethylene glycol diethyl ether (in triglyme) were used as internal standards. Pseudo-first-order rate constants (k_{obs}) were evaluated as for aniline. The results are reported in Table 2.

For a convenient comparison, Table 2 also reports the result for **1a** and an estimate of the molecular size of amines **1a**, **1b**, and **1b′** expressed through the dimensions *x*, *y*, and *z* of the smallest box able to fit in such compounds (columns 3−5; see also the Experimental Section).

(17) Espeel, P. H. J.; Vercruysse, K. A.; Debaerdemaker, M.; Jacobs, P. A. *Stud. Surf. Sci. Catal.* **1994**, *84*, 1457.

(18) Jayat, F.; Sabater Picot, M. J.; Guisnet, M. *Catal. Lett.* **1996**, *41*, 181.

(19) Zeolites are known to be hygroscopic solids. Before each reaction, the catalyst was dried with heating overnight at 70 °C and under vacuum (10 mm). This treatment was not applied in the case of entry 3 in Table 1. The dried zeolite showed a weight decrease in the range of 5−7% (determined through a gravimetric comparison between three dried and nondried samples).

TABLE 3. Methylation of *p*-Alkylanilines 1c−e and Di- and Tri-*tert*-butyl-Substituted Anilines 1f,g with the Carbonate 2a[a]

entry	amine	x (Å)	y (Å)	z (Å)	zeolite hosting ability[b]	solvent	T (°C)	t (h)	convn (%)	$S_{M/D}$ (%)	product (M + D) yield[d] (%)
1	aniline, **1a**	4.34	1.17	5.59	yes	xylene	130	4	100	99	96
2	*p*-toluidine, **1b**	4.34	1.81	6.44	yes	xylene	130	7	66	94	66
3	*p*-ethylaniline, **1c**	4.64	1.91	8.08	yes	xylene	130	8	41	92	41
								24	68	91	65
4	*p*-propylaniline, **1d**	4.67	1.90	9.20	yes	xylene	130	8	27	89	27
								24	45	90	44
5	*p*-butylaniline, **1e**	4.81	1.93	10.62	yes	xylene	130	8	9	92	9
6	3,5-di-*tert*-butylaniline, **1f**	6.56	4.38	8.71	c	triglyme	160	7	9	82	6
7	2,4,6-tri-*tert*-butylaniline, **1g**	9.20	4.39	8.42	no	triglyme	160	8			

[a] Except for aniline (see entry 1, Table 1), all reactions were run using solutions of the substrates in xylene or triglyme (0.3 M, 5 mL). The molar ratio **2a**:**1** was 5. The weight ratio NaY:**1** was 0.5. All data were averaged over two consecutive runs. [b] The hosting ability was referred to as the possibility to fit the reagent into the zeolite cage, through the estimate of dimensions x, y, and z. [c] The size of compound **1f** makes uncertain its diffusion through the zeolite channels (d = 7.4 Å). [d] Percentage of mono-*N*-methyl and di-*N*,*N*-methyl derivatives.

In xylene as the solvent, the more nucleophilic amines **1b** and **1b′** show a comparable reactivity (entries 2 and 3), but surprisingly, their methylation reactions appear much slower and even less selective with respect to aniline:[20] this is especially true for *p*-anisidine ($S_{M/D}$ = 85%, at 56% conversion; entry 3).

As for aniline, the reaction rate is also slowed with the increase of the solvent polarity (compare entries 3 and 4 and entries 5 and 6), though the selectivity is slightly improved (entries 3 and 6).

The steric requisites of **1b** and **1b′** (x, y, z) indicate that these compounds should have relatively free access to the catalytic cages: Y faujasites possess, in fact, inner pores (supercages) 11.8 Å in diameter, which are connected through channels 7.4 Å in diameter.[21] If so, the drop of the reaction rate observed for *p*-toluidine and *p*-anisidine would be mainly due to electronic effects of aryl substituents. Both amines **1b** and **1b′** may diffuse and adsorb into the catalyst following the pattern proposed for aniline, with two sites of adsorption:[22] on the first, the amine is held through H-bonds between amine protons and basic oxygen atoms of the zeolitic framework; on the second, the amine is pinned to the lattice, forming a π complex between the aryl ring and an acid cation (e.g., Na$^+$). Since the strength of these interactions increases for electron-rich anilines, the desorption of *p*-toluidine and *p*-anisidine as well as their mono-*N*-methyl derivatives is expected to be less favored with respect to aniline. This would account not only for the decrease of the rate, but also for the drop of selectivity described in Table 2.

However, although this electronic effect is relevant, the bulkiness of the aryl substituents plays an important role as well. This clearly emerges from the following experiments.

***p*-Alkylanilines**. At 130 °C, solutions of *p*-alkylanilines **1c−e** in xylene (0.3 M, 5 mL) were made to react with the carbonate **2a** (**2a**:**1** in a 5:1 molar ratio) in the presence of NaY (NaY:**1** in a 0.5:1 weight ratio). *n*-Dodecane was used as the internal standard. In this case,

the reactivity of different amines was compared through the evaluation of reaction conversions rather than kinetic constants.[23]

Moreover, also highly hindered amines such as 3,5-di-*tert*-butyl- and 2,4,6-tri-*tert*-butylanilines (compounds **1f,g**, respectively) were used as the substrates. At 160 °C, they were made to react with **2a** in tryglime as the solvent under the conditions used for *p*-alkylanilines.

The results are reported in Table 3. As for Table 2, the dimensions x, y, and z of the smallest box able to fit in the amines **1a−g** are also reported (columns 3−5).

The data show that the increase of the steric hindrance of the substituents immediately reflects on the reaction rate: in going from the *p*-methyl to the *p*-butyl group, the conversion drops from 66% to 9% after reaction times of 7 and 8 h (entries 2−5). Yet, as far as the reactant amines are allowed to migrate into the catalytic cages, the mono-*N*-methyl selectivity is rather constant (90−94%) at comparable conversions (entries 2−5).

The effect is much more drastic for compounds **1f−g**. 3,5-Di-*n*-butylaniline, whose diffusion (if any) into the catalyst is severely hampered, undergoes a sluggish reaction even at 160 °C (entry 6), and despite the very low conversion (9%), the selectivity is only 82%: byproducts of N,N-dimethylation (1%) and N-alkylation (ArNHR, R = MeO(CH$_2$)$_2$O(CH$_2$)$_2$; 3%] reactions are observed. This decrease of selectivity can also be ascribed to the reaction taking place on the external surface of the zeolite.

Under the same conditions, 2,4,6-tri-*n*-butylaniline (**1g**), which cannot access the inner pores of the zeolite, does not react (entry 7). Given the steric crowding around the amine function, it is also in doubt whether compound **1g** would be able to react at all with the carbonate.

***p*-Alkoxyanilines**. Previous experiments on **1b′** (Table 2) suggested that selectivity could be improved in the presence of triglyme as the solvent. Moreover, reactions in triglyme could be run at a higher temperature with respect to xylene: this would have helped the investigation of more hindered alkoxyanilines whose reactivities were expected to be lower than that of **1b′**. Accordingly, solutions of *p*-alkoxyanilines **1c′−e′** in triglyme (0.3 M,

(20) Although aniline was made to react in a more concentrated solution (0.4 M, Table 1) with respect to **1b** and **1b′** (0.3 M), this difference could not account for the observed variation of k_{obs} (entries 1−3).

(21) Schwochow, F.; Puppe, I. *Angew. Chem., Int. Ed. Engl.* **1975**, *14*, 620.

(22) Czjiek, M.; Vogt, T.; Fuess, H. *Zeolites* **1991**, *11*, 832.

(23) Some of the investigated amines were quite unreactive, and the corresponding k_{obs} values were not determinable.

TABLE 4. Methylation of *p*-Alkoxyanilines 1b′–1e′ with 2-(2-Methoxyethoxy)ethyl Methyl Carbonate[a]

entry	amine	x (Å)	y (Å)	z (Å)	zeolite hosting ability[b]	t (h)	convn (%)	$S_{M/D}$ (%)	product (M + D) yield[c] (%)
1	**1b′**	4.60	1.86	7.89	yes	5	73	86	70
						8	84	78	80
2	**1c′**	4.59	1.83	9.03	yes	8	43	92	42
						23	81	80	78
3	**1d′**	4.73	1.89	10.44	yes	8	22	93	22
						23	55	85	54
4	**1e′**	4.72	1.89	11.63	yes	8	9	95	9

[a] All reactions were run at 150 °C using solutions of the substrates (0.3 g) in triglyme (5 mL). The molar ratio **2a**:**1** was 5. The weight ratio NaY:**1** was 1. All conversion data were averaged over two runs. [b] Defined as in Table 3. [c] Percentage of mono-N-methylated and di-N,N-methylated products.

5 mL) were made to react at 150 °C with the carbonate **2a** (**2a**:**1** in a 5:1 molar ratio) in the presence of NaY (NaY:**1** in a 1:1 weight ratio). *n*-Tetradecane was used as the internal standard. The reactivities of different amines were compared through the evaluation of reaction conversions rather than kinetic constants. All products were identified by GC/MS analyses.

The results are reported in Table 4.

Although a direct comparison between Tables 3 and 4 is not possible, *p*-alkoxyanilines show the same trend as described for *p*-alkylanilines. The increase of steric hindrance of *para*-substituents (from *p*-MeO to *p*-BuO groups) results in a striking drop of the reaction conversion (from 84% to 9% after 8 h; entries 1–5).

Also the mono-*N*-methyl selectivity is comparable between the two sets of amines (*p*-alkyl and *p*-alkoxy amines) when their bulkiness is considered. For example, *p*-propyl- and *p*-ethoxyanilines, for which very similar molecular sizes are estimated (see *x*, *y*, and *z* of entries 4 in Table 3 and 2 in Table 4), show $S_{M/D}$ values of 90% and 92% at conversions of 45% and 43%, respectively. Likewise, *p*-butyl- and *p*-propoxyanilines exhibit an analogous behavior (entries 5 of Table 3 and 3 of Table 4).

On the whole, the data of Tables 2–4 are all consistent with the following facts: (i) Steric effects are crucial for the reaction rate. The methylation rate of *para*-substituted anilines is markedly slower with larger substituents, but as long as the diffusion of amines is allowed into the catalytic supercages of NaY, the reaction may take place with comparable mono-*N*-methyl selectivities (at similar conversions) for all the tested substrates. Otherwise, if diffusion is inhibited or severely limited, the reaction hardly occurs and selectivity drops as well.

(ii) Within limits, the more nucleophilic the amine is, the slower its reaction is as well. Electronic effects of the substituents alter the rate of adsorption/desorption of both reagents and products into the catalyst. This seems to affect primarily the methylation rate, but also influences selectivity: the geometric features of the zeolite cage can shape the formation of the mono-*N*-methyl derivative on the condition that the migration of reagent and product through the catalytic pores is not hampered by electronic effects. (iii) Although preliminary, the estimation of the molecular size of the reactants through the simple device of the smallest box seems to offer a good

SCHEME 3. Selective Mono-N-methylation of Anilines with DMC[a]

$$ArNH_2 + MeOCO_2Me \longrightarrow ArNHCO_2Me + MeOH \quad (a)$$
$$\mathbf{1} \qquad\qquad\qquad\qquad \mathbf{4}$$

$$ArNHCO_2Me + Z \longrightarrow ArN^{(-)}CO_2Me + HZ^{+} \quad (b)\,^*$$

$$ArN^{(-)}CO_2Me + DMC \longrightarrow ArN(Me)CO_2Me + MeOCO_2^{-} \quad (c)$$
$$\mathbf{5}$$

$$ArN(Me)CO_2Me + MeOH \longrightarrow ArNHMe + DMC \quad (d)$$

$$MeOCO_2^{-} + HZ^{+} \longrightarrow MeOH + CO_2 + Z \quad (e)$$
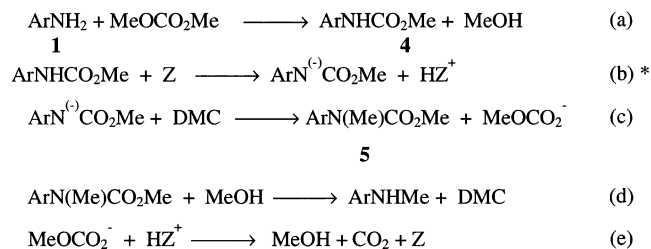
[a] The asterisk indicates that Z is a basic site of the zeolite.
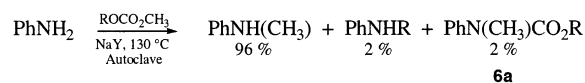
prediction of the reaction outcome as both rate and selectivity are concerned.

Mono-N-methylation of Anilines. Reaction Mechanism. In a preliminary mechanistic investigation, the mono-*N*-methyl selectivity of the reaction of anilines with DMC has been explained through Scheme 3.[2]

An amine (**1**) is initially adsorbed into a zeolite cage, where it reacts with DMC to form a carbamate [ArNHCO$_2$-Me (**4**), eq a]. Due to its polarity, the corresponding anion **4**$^-$ is held into the zeolite pores where both methylation and demethoxycarbonylation reactions take place (eqs c and d). Two observations strengthen this mechanistic scheme: (i) the occurrence of small amounts (1–5%) of compound **4** and ArN(Me)CO$_2$Me (**5**) in the reaction of anilines with DMC; (ii) when PhNHCO$_2$Me was made to react with DMC, it was first converted into PhN(Me)-CO$_2$Me, which in turn gave PhNHMe.

This mechanism sounded reasonable also for the reactions of anilines with the carbonate **2a**. However, all the attempts to confirm the presence of the corresponding carbamates ArNHCO$_2$R and/or ArN(Me)CO$_2$R (R = MeO-(CH$_2$)$_2$O(CH$_2$)$_2$) failed.

Apparently, the only striking difference between the reactions of DMC and of the carbonate **2a** was that the former was reacted in a closed vessel (autoclave), while the latter was reacted at atmospheric pressure. To rule out such a distinction, aniline was also made to react at 130 °C with **2a** (**1a**:**2a** in a 1:9 molar ratio) in an autoclave in the presence of NaY (weight ratio NaY:**1a** = 1). Under these conditions, the carbamate **6a** [PhN-(Me)CO$_2$R, R = MeO(CH$_2$)$_2$O(CH$_2$)$_2$] was finally observed in a 2% yield (Scheme 4).[24]

SCHEME 4. Reaction of Aniline with the Carbonate 2a: Composition of the Reaction Mixture after 5 h at 130 °C

$$PhNH_2 \xrightarrow[\substack{NaY, 130\,°C \\ Autoclave}]{ROCO_2CH_3} PhNH(CH_3) + PhNHR + PhN(CH_3)CO_2R$$
$$96\,\% \qquad 2\,\% \qquad 2\,\%$$
$$\mathbf{6a}$$

This result not only supported the similarity of the reaction mechanism of DMC and of the carbonate **2a**, but also suggested that the presence of the intermediate carbamates **4**–**6** (formed reversibly through reactions a, c, and d of Scheme 3) could be controlled by the CO$_2$ released from the reaction. For this reason, the demethoxycarbonylation reaction of these moieties could perhaps

(24) The product **4a** was characterized by GC/MS analysis of the reaction mixture. The structure was then confirmed by its synthesis from the transesterification of PhN(Me)CO$_2$Me with MeO(CH$_2$)$_2$O-(CH$_2$)$_2$OH catalyzed by K$_2$CO$_3$ (see the Experimental Section).

be faster at atmospheric pressure. A beneficial effect of the CO_2 pressure has been recently reported by us also in the synthesis of methyl carbamates from aliphatic amines and DMC.[25] However, there are presently no clear reasons why the formation of compound **6a** was so chemoselective (not even a trace of $PhN(Me)CO_2Me$ was detected).

Finally, it should be noted that if Scheme 3 applies, the relationship among the rate constants for methoxy-carbonylation (a), methylation (c), and demethoxycarbo-nylation (d) reactions may also control selectivity, and explain the first-order disappearance observed for aniline (Figure 2), which may appear even too simple given Scheme 3.

N-Methylation of Benzylamine. In general, the reactions of primary aliphatic amines with conventional alkylating agents are much less selective than those of anilines.[26] We experienced this behavior also in the use of dimethyl carbonate as a methylating agent:[2] for example, at 130 °C, the reaction of benzylamine with DMC catalyzed by NaY yielded the corresponding mono-*N*- and di-*N,N*-methyl derivatives in equal amounts even at very low conversions (≤10%).

With the aim of improving the mono-*N*-alkyl selectivity of such processes, two facts could be exploited: (i) the high basicity and nucleophilicity of aliphatic amines could be used to run reactions under milder conditions; (ii) the amphoteric properties of Y faujasites were tunable (by changing their metal cations).[27] Accordingly, the use of different MY zeolites (M = Li, Na, K, Cs) could have modified the reaction outcome.

Initial experiments were carried out at 90 °C and atmospheric pressure. Benzylamine (**7**; 0.3 g, 2.8 mmol) was made to react with either dimethyl carbonate (20 mL, as a reagent/solvent) or the carbonate **2a** (xylene solutions, 0.4 M, 5 mL; **2a**:**7** in a 5:1 molar ratio) in the presence of NaY (weight ratio NaY:**7** = 1). For comparison, the reaction with **2a** was also run at 130 °C.

The results are reported in Table 5.

In the case of DMC, it should be first noted that the mono-*N*-methyl selectivity—although not as satisfactory as for anilines—is significantly improved with respect to previous results at a higher temperature:[2,28] on NaY, $S_{M/D}$ increases from 38% (at 130 °C, entry 2) to 63% (at 90 °C, entry 1b) at comparable conversions (75% and 67%). To our knowledge, the best procedure for the direct mono-N-alkylation of benzylamine claims selectivities up to 85%, though only with sparingly reactive alkyl bromides RBr (R = n-C_4H_9 and n-C_8H_{17}).[29]

As for DMC, also in the case of the carbonate **2a**, the reaction temperature has a drastic effect on the monoalkyl selectivity: at comparable conversions (46–49%), $S_{M/D}$ is 75% and 63% at 90 and 130 °C, respectively (entries 3 and 4).

In view of these data, the N-methylation of benzyl-amine was investigated in the presence of DMC and a

TABLE 5. N-Methylation of 7 with DMC and 2a in the Presence of MY Catalysts

entry	MY	ionic exchange[a] (%)	carbonate[b]	T (°C)	t (h)	convn (%)	$S_{M/D}$[c] (%)	product yield[d] (%) M	D
1a	NaY		DMC	90	7	44	84	34	7
1b	NaY		DMC	90	22	67	63	42	20
2[28]	NaY		DMC	130	3.5	75	38	26	43
3a	NaY		**2a**	90	22	13	85	11	22
3b	NaY		**2a**	90	94	46	75	33	10
4	NaY		**2a**	130	22	49	63	29	17
5a	LiY	82	DMC	90	7	43	84	34	9
5b	LiY	82	DMC	90	22	70	63	41	24
6a	KY	81	DMC	90	7	18	91	16	2
6b	KY	81	DMC	90	22	33	79	24	7
7a	CsY	56	DMC	90	7	19	92	17	2
7b	CsY	56	DMC	90	22	36	77	26	8

[a] Percentage of ionic exchange from NaY: the metal contents were evaluated through atomic adsorption (Na, K) and emission (Li, Cs). [b] For entries 1–4, DMC was used as a reagent/solvent (20 mL); for entry 5, a solution of benzylamine (0.4 M, 5 mL) in xylene was made to react with **2a** (**2a**:**7** = 5 molar ratio). n-Tetradecane was the internal standard. [c] $S_{M/D}$ = mono-*N*-methyl selectivity defined as in Tables 2–4. [d] M = mono-*N*-methylben-zylamine and D = di-*N,N*-methylbenzylamine.

series of MY zeolites (M = Li, Na, K, Cs) under the conditions previously described (**7**, 0.3 g; DMC, 20 mL; weight ratio MY:**7** = 1).[30] These catalysts were prepared by exchange of NaY with aqueous solutions of alkali-metal salts.

The results are also reported in Table 5.

Both the reaction rate and selectivity appear markedly affected by the nature of the catalyst, and in general, LiY and NaY faujasites allow more rapid and selective reactions with respect to KY and CsY. After 7 h, reactions with LiY/NaY show benzylamine conversions up to 44% with an $S_{M/D}$ of 84% (entries 1a and 5a), while with KY/CsY conversions are lower (33–36%) even after 22 h. Despite that, $S_{M/D}$ ratios are lower as well (77–79%, entries 6b and 7b).

Figure 4 describes this situation in more detail for the LiY and CsY catalysts: when selectivity is reported vs conversion, the formation of mono-*N*-methylbenzylamine on LiY is better than on CsY. The effect of the Cs ion is even more surprising if one considers that CsY is actually a "mixed zeolite" which contains almost equal amounts of Cs^+ and Na^+ (Table 5, entry 7, ionic exchange of 56%).

The acid/base features of MY and the size of the metal cations seem to be the rationale for the results of Table 5 and Figure 4.

The basicity of these catalysts (due to the oxygen atoms of the zeolitic framework) can be increased by exchange with soft metal cations, and it follows the order Cs > Rb > K > Na > Li.[27] The Lewis acidity instead (due to metal cations) goes through the reverse sequence, and is higher for LiY.[27,31] In our case, the more acidic the zeolite, the better the reaction selectivity as well: the increased acidity may lower the nucleophilic character of the

(25) Selva, M.; Tundo, P.; Perosa, A. *Tetrahedron Lett.* **2002**, 1217–1219.

(26) Smith, J. W. In *The Chemistry of the Amino Group*; Patai, S., Ed.; Interscience: London, 1968; Chapter 4.

(27) Barthomeuf, D. *J. Phys. Chem.* **1984**, *88*, 42.

(28) Berto, C. Thesis, University of Ca' Foscari, Venezia, Italy, 2001.

(29) Salvatore, R. N.; Nagle, A. S.; Jung, K. W. *J. Org. Chem.* **2002**, *67*, 674–683.

(30) The carbonate **2a** was advantageous for high-temperature methylation reactions ($T > 120$ °C). However, since benzylamine was rapidly methylated also at a lower temperature (90 °C), DMC (a commercially available compound) could be used more conveniently at its reflux temperature (90 °C) and at atmospheric pressure.

(31) (a) Rao, J. V. *Chem. Commun.* **1998**, 269. (b) Su, B.; Barth-omeuf, D. *Stud. Surf. Sci. Catal.* **1995**, *94*, 598. Actually, ref 31b reports that Y faujasites possess only Lewis-type acidity, the Brönsted contribution of OH groups on the surface being negligible.
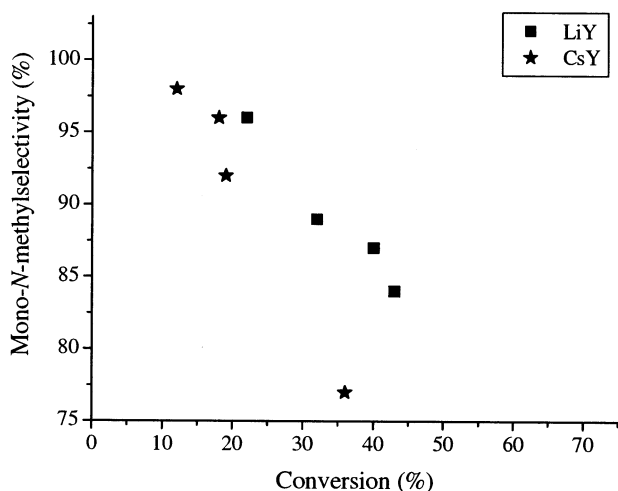
FIGURE 4. Reaction of benzylamine with DMC in the presence of LiY and CsY faujasites: mono-*N*-methyl selectivity vs conversion.

reactant amine so that N,N-dimethylation is disfavored. Also in the methylation of aniline with MeOH, it has been reported that LiY/NaY faujasites can catalyze both ring alkylation and N-alkylation reactions, while KY/CsY exclusively directs the reaction toward N-methylation.[32]

Steric hindrance of the metal cations may account for effects on the reaction rate. The drop of conversions observed with KY and CsY is reasonably due to the larger size of K$^+$/Cs$^+$ (with respect to Li$^+$/Na$^+$):[33] these moieties may partially obstruct the zeolite channels in a way that the diffusion of reactants is hindered.

From a mechanistic viewpoint, the occurrence of methyl carbamates [both PhCH$_2$NHCO$_2$Me and PhCH$_2$N-(Me)CO$_2$Me were observed in a 1−5% total yield) indicates that the pattern sketched out in Scheme 3 is perhaps active for benzylamine too. Though, the lower selectivity with respect to anilines cannot rule out a B$_{Al}$2-type reaction where the amine directly attacks the methyl group of DMC.

Conclusions

In the presence of Y faujasites, the investigation of the mono-*N*-methyl selectivity in the reactions of primary amines with methyl alkyl carbonates allows the following considerations.

(i) Aniline. At 130 °C and atmospheric pressure, the liquid-phase methylation of aniline—the model compound for aromatic amines—with the carbonate **2a** can be run with NaY under conditions free from diffusion limitations. Accordingly, the kinetic investigation of this reaction shows a clear effect of the solvent polarity: the rate constant decreases by a factor of 5 when the dielectric constant of the solvent increases from 2.40 (xylene) to 7.62 (triglyme). More polar solvents (DMF) inhibit the reaction. Competitive adsorption phenomena between the amines and the solvent for the active sites of the catalyst offer a good rationale for this behavior. Notwithstanding,

much remains to be understood of the adsorption and activation of the organic carbonates.

A mechanistic similarity is plausible for the reactions of **2a** and DMC. Although preliminary, this is based upon the intermediacy of carbamate species whose formation is probably dependent on the CO$_2$ pressure generated throughout the reaction.

(ii) *p*-Alkyl- and *p*-Alkoxyanilines. With respect to scantly nucleophilic aromatic amines, the reaction of *p*-alkyl- and *p*-alkoxyanilines with **2a** presents some synthetic limitations: the mono-*N*-methyl selectivity does not exceed 80% at conversions up to 85%. However, this investigation sheds light on the relationship between the steric demand of the zeolite cages and the steric/electronic effects of *para*-substituents. In particular, the shape of the zeolite pores may affect the mono-*N*-methyl selectivity, provided that the diffusion of reagents into the catalyst is fast enough. Accordingly, as long as the diffusion of these substrates is inhibited, both the selectivity and rate drop markedly.

(iii) Benzylamine. The reaction of benzylamine—a model for aliphatic amines—with both DMC and the carbonate **2a** provides further insight for the improvement of the mono-*N*-methyl selectivity. By varying the amphoteric properties of the catalysts—in particular, by increasing their acid strength with the use of hard cations (Li$^+$ and Na$^+$)—better selectivity (due perhaps to the modification of the nucleophilicity of the amine) and reaction rate (due to the lesser hindrance of small ions) are achieved.

In view of this outcome, a further step in this area will be the preparation and use of faujasites in the protonic form (HY and HX).

Overall, this work has shown some of the main features of the methylation of primary amines with methyl alkyl carbonates and DMC, catalyzed with alkali-metal-exchanged Y faujasites. The scenario is rather complex: the size of the amines feels the geometry of the catalyst, but the final mono-*N*-methyl selectivity arises from a synergic effect between the double reactivity of organic carbonates (as methoxy/alkoxy carbonylating and methylating agents) and the steric—amphoteric requisites of the zeolite cages.

Experimental Section

All compounds used were ACS grade and were employed without further purification. The zeolite NaY was available commercially. 2-(2-Methoxyethoxy)ethyl methyl carbonate [MeO(CH$_2$)$_2$O(CH$_2$)$_2$OCO$_2$Me, **2a**] was prepared according to a procedure already reported and compared to an authentic sample.[4] ^{1}H NMR spectra were recorded on a 300 MHz spectrometer, using CDCl$_3$ with TMS as the internal standard. GLC and GC/MS (70 eV) analyses were run using 30 m capillary columns.

4-Propoxyaniline (1d′) was synthesized from *p*-nitrophenol according to known procedures.[34] ^{1}H NMR (CDCl$_3$): δ 6.76 (2H, d, *J* = 8.7 Hz, Ar), 6.65 (2H, d, *J* = 8.7 Hz, Ar), 3.86 (2H, t, *J* = 6.7 Hz, −OCH$_2$−), 3.33 (2H, br s, NH$_2$), 1.78 (2H, tq, *J*$_1$ = 6.7 Hz, *J*$_2$ = 7.6 Hz, −CH$_2$C*H*$_2$CH$_3$), 1.03 (3H, t, *J* = 7.6 Hz, CH$_3$). GC/MS (70 eV): *m*/*z* 151 (M$^+$, 24), 109 ([M − CH$_2$=

(32) Su, B. L.; Barthomeuf, D. *Appl. Catal., A* **1995**, *124*, 73.
(33) Greenwood, N. N.; Earnshaw, A. *Chemistry of the Elements*; Pergamon Press: New York, 1984.

(34) (a) Norman, R. O. C. *Principles of Organic Synthesis*, 2nd ed.; Chapman & Hall: New York, 1989; pp 426−427. (b) Willson, F. G.; Wheeler, T. S. *Organic Synthesis*; Wiley: New York, 1955; Collect. Vol. III, p 140. (c) Ozeki, K.; et al. *Chem. Pharm. Bull.* **1989**, *37* (7), 1780.

$CHCH_3]^+$, 100), 108 (33), 81 ([(M − CH_2=$CHCH_3$) − $CO]^+$, 9), 80 (42). IR (neat), cm^{-1}: 3354 (NH_2), 1236 (C−O−C).

Reaction of Aniline with 2a. Figure 2 and Table 1. A three-necked, jacketed, 25 mL round-bottomed flask fitted with a stopcock, an adapter for the withdrawal of samples, a reflux condenser capped with a N_2-containing rubber reservoir, and a magnetic bar was loaded with a solution of aniline (**1a**) (0.4 M, 5 mL) in a given solvent; in particular, xylene, triglyme, and *N,N*-dimethylformamide were used. *n*-Tetradecane (0.6 mmol) or ethylene glycol di-*n*-hexyl ether (*n*-$C_6H_{13}$$OCH_2CH_2O$-*n*-$C_6H_{13}$; 0.45 mmol) was used as the internal standard for reactions with xylene/triglyme or DMF, respectively.

The organic carbonate **2a** [$MeOCO_2$(CH_2)$_2$O(CH_2)$_2$OMe] and the faujasite NaY were added to the mixture (**2a**:**1a** = 5 molar ratio, **1a**:NaY = 0.5 weight ratio), which was then degassed under vacuum and put under a N_2 atmosphere. The flask was heated at the desired temperature (130 °C) while the mixture was vigorously stirred. At intervals, samples (0.1 mL) were withdrawn and were analyzed by both GC and GC/MS.

Under these conditions, a reaction was also performed without any solvent and in the presence of ethylene glycol di-*n*-hexyl ether as the internal standard.

Figure 1, Tables 2−5. The above-described procedure was followed also for the experiments of Figure 1 and Tables 2−5 according to the molar and weight ratios reported there.

All reactions except those of amines **1f**−**g** in Table 3 were carried out in the presence of an internal standard, which was (a) *n*-dodecane for reactions of *p*-alkylanilines or (b) *n*-tetradecane for reactions of *p*-alkoxylanilines and benzylamine. The molar ratio amine:standard was 2.5. Accordingly, calibration curves were built for each substrate, and used to follow the reaction by GC. In the case of aniline, a calibration curve was also made for the product *N*-methylaniline.

Table 5. Reactions with DMC. Under the conditions described above, benzylamine (0.3 g) was also made to react at 90 °C with DMC (20 mL) in the presence of different MY catalysts (M = Li, Na, K, Cs; **7**:MY= 1 weight ratio). *n*-Tetradecane was the internal standard. The molar ratio amine: standard was 2.5.

If not otherwise indicated, all reactions were repeated at least twice, and the data of the kinetic constants or conversions were averaged over two runs not differing more than 10% from each other.

N-Monomethyl and *N,N*-dimethyl derivatives of the investigated amines were identified by GC/MS. The methylated products of aniline, *p*-toluidine, *p*-ethylaniline, *p*-anisidine, and benzylamine (RNHMe, **3a**−**c**, **3b′**, and **8**; RNMe₂, **9a**−**c**, **9b′**, and **10**) were confirmed by comparison with authentic commercial samples. GC/MS spectra of all the other compounds are available in the Supporting Information.

Ethylene Glycol Di-*n*-hexyl Ether. This compound was prepared according to known procedures.[35] The use of this standard was convenient for both its high boiling point and solubility in polar solvents.

Reaction of Aniline in an Autoclave. A stainless steel autoclave (150 mL of internal volume) was charged with aniline, the carbonate **2a** (**1a**:**2a** = 9 molar ratio), and NaY (**1a**:NaY = 1 weight ratio). At rt and before the reaction, air was removed by a purging valve with a N_2 stream. The autoclave was then heated by an oil-circulating jacket while the mixture was kept under magnetic stirring. A thermocouple fixed onto the autoclave head checked the temperature throughout the reaction. After 5 h, the autoclave was cooled to rt, purged from CO_2, and finally opened. The reaction mixture was analyzed by GC and GC/MS.

Estimation of the Molecular Size of Amines 1a, 1b−g, and 1b′−e′. The dimensions (*x*, *y*, *z*) of the smallest boxes able to fit compounds **1a**, **1b**−**g**, and **1b′**−**e′** were estimated with the use of Hyperchem Pro ver. 5.11. The calculation method was molecular mechanics using the MM+ force field (options electrostatic potential = bond dipoles, and cutoff = none), and the type of calculation was geometry optimization performed through the conjugate gradient method [Polak−Ribiere algorithm with an RMS (root-mean-square) gradient of 0.1 kcal/ (Å mol)].

Carbamates. *N*-Benzyl methyl carbamate ($PhCH_2NHCO_2$-Me, **7a**[36]) and *N*-methyl-*N*-benzyl methyl carbamate [$PhCH_2N$-(Me)CO_2Me, **7b**[37]] were prepared according to known procedures.[38] The synthesis of **6a** [PhN(Me)CO_2R, R = MeO(CH_2)$_2$O-(CH_2)$_2$] was performed by adjusting a known transesterification reaction of *N*-phenyl methyl carbamate with alcohols:[39] a jacketed, 25 mL round-bottomed flask was charged with *N*-methyl-*N*-phenyl methyl carbamate [PhN(Me)CO_2Me; 0.2 g, 1.2 mmol], diethylene glycol monomethyl ether [MeO-(CH_2)$_2$O(CH_2)$_2$OH; 10 mL], and K_2CO_3 (0.83 g, 6 mmol). The mixture was magnetically stirred and heated at 130 °C. After 25 h, the carbamate **6a** was observed in a very low yield (2%). No other products were obtained. Compound **6a** was characterized by GC/MS analysis (70 eV): *m/z* 253 (M^+, 20), 195 ([M − CH_2=$CHOCH_3]^+$, 13), 179 ([(M − CH_2=$CHOCH_3$) − $O]^+$, 31), 151 ([M − CH_2=CHO(CH_2)$_2$$OCH_3]^+$, 100), 135 ([(M − CH_2=CHO(CH_2)$_2$$OCH_3$) − $O]^+$, 65), 107 (29), 106 ([M − CO_2-(CH_2)$_2$O(CH_2)$_2$$OCH_3]^+$, 49), 77 (44).

MY Catalysts. (a) Preparation and Characterization. Faujasites MY (M = Li, K, Cs) were prepared by an ionic exchange reaction of the commercially available NaY with aqueous solutions of MCl.[40] The metal content of the catalysts was determined as follows: A Teflon-lined autoclave (200 mL) was charged with MY (0.1 g), milli-Q water (5 mL), aq HF (40%, 1.5 mL), and a mixture of aq HCl/HNO_3 (3:1 v/v; 3 mL). The autoclave was then closed with a Teflon-lined cap, and heated in a microwave digestion rotor for 20 min (power ranging from 250 to 650 W). After being cooled to rt, the clear solution was transferred into a volumetric flask and diluted with milli-Q water to 50 mL. Then, analyses by atomic adsorption [λ(Na) = 589.0 nm; λ(K) = 766.5 nm] and emission (Li, Cs) were performed according to known procedures.[41]

(b) Treatment. If not otherwise specified, before each reaction, all the catalysts MY were dehydrated by being heated at 65 °C under vacuum (10 mmHg) overnight.

Dielectric Constant of 2a. The dielectric constant of **2a** was measured by a capacitor with circular plates (C_{meas}) inserted into the circuit shown in Scheme 5.

SCHEME 5[a]
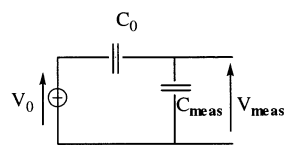
[a] V_0 = 200 mV; C_0 = 255 pF.

By applying a potential V_0 of 200 mV, and with a capacitor C_0 of 255 pF, the capacity of C_{meas} was alternatively measured in air and after dipping the capacitor into the carbonate **2a** (eq 3). Finally, the wanted dielectric constant was calculated from $\epsilon_r = C_{2a}/C_{air} = 352/57 = 6.2$.

$$C_{meas} = C_0\left(\frac{V_0}{V_{meas}} - 1\right) \quad (3)$$

(36) Kost, D.; Zeichner, A.; Sprecher, M. *J. Chem. Soc., Perkin Trans. 2* **1980**, 317.
(37) Cox, C.; Lectka, T. *J. Org. Chem.* **1998**, *63*, 2426.
(38) (a) Iwakura, Y.; Izawa, S. I. *J. Org. Chem.* **1964**, *29*, 379. (b) Kost, D.; Zeichner, A.; Sprecher, M. *J. Chem. Soc., Perkin Trans. 2* **1980**, 317.
(39) Derouane, E. G. *J. Mol. Catal., A* **1998**, *134*, 95.
(40) Onaka, M.; Ishikawa, K.; Izumi, Y *Chem. Lett.* **1982**, 1783.
(41) *Analytical Methods Manual*; Varian Inc.: 1989.

(35) Klocke, E.; Matzeit, A.; Gockein, M.; Schäfer, H. *Chem. Ber.* **1993**, *126*, 1623.

Supporting Information Available: GC/MS spectra for compounds **3d,e,f,c′,d′,e′** and **9d,e,f,c′,d′,e′**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO026057G