

SELECTIVE N-MONOALKYLATION OF ANILINE DERIVATIVES BY USE OF ALKALI
CATION EXCHANGED X- AND Y-TYPE ZEOLITES

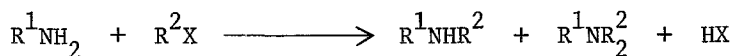
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ABSTRACT. Alkali cation exchanged X- and Y-type zeolites are employed to promote the reactions of aniline derivatives with alkylating agents in organic solvent. The N-alkylation is accelerated by the cooperative function of the acid and base sites on the potassium cation exchanged X- and Y-type zeolites to give the N-monoalkylated product in very high selectivity. Especially the use of the zeolite is found to be effective for N-alkylation of deactivated aromatic amines like nitroaniline. The highly selective N-monoalkylation is attributed to the reaction occurring inside the homogeneous narrow cavities of zeolites.

1. INTRODUCTION

Recently there have been reported a lot of organic syntheses over inorganic oxides such as silica gel and alumina in the liquid phase [1]. These heterogeneous organic reactions are thought to be promoted by the acid or base sites on the surface of inorganic oxides. Among various inorganic oxides we are particularly interested in well-defined crystalline aluminosilicate zeolite, because various cation exchanged zeolites have been employed as acid or base catalysts and the intrinsic homogeneous cavities in the zeolite discriminate the molecular shapes of reactants, reactive intermediates, or products [2]. Although many investigations on catalytic behavior of zeolite have been undertaken mainly for the gas-phase reactions, little study has been made on the utilization of zeolite in the liquid-phase organic reactions.

The reaction of primary amine with an equimolar amount of alkylating agent is known to proceed under basic reaction conditions to give a mixture of N-monoalkylated and N,N-di-alkylated amines. We employed zeolite in the reactions of aniline derivatives with alkylating agents in organic solvents to investigate both the effectiveness of zeolite as acid and/or base and the ability in enhancing the product selectivity.



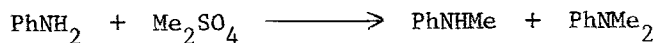
2. MATERIALS AND METHODS

The solvents were dried over molecular sieve 3A. The zeolites Linde 13X (abbreviated as NaX) and Linde 13Y (NaY) were purchased from Shokubai Kasei Co., Ltd. Various ion exchanged zeolites were prepared according to the ion exchange technique: Powdered zeolite (100 g) was immersed in an aqueous 0.5 M solution of the corresponding metal chloride (1000 ml) at 70 °C for 3 h, and then the aqueous solution was decanted off. This procedure was repeated 10 times. Next, the ion exchanged zeolite was washed with deionized water until no chloride ion was detected in the filtrate, and dried at 110 °C for 10 h, then at 500 °C for 5 h in air. The content of the exchanged cation in the zeolite was determined by means of atomic absorption analysis.

N-Alkylation of anilines was carried out under an argon atmosphere. A mixture of aniline and zeolite was stirred in organic solvent for 1 h at room temperature, and then the alkylating agent was added. The resulting mixture was stirred under the conditions shown in the tables. To the reaction mixture was added water and the resulting mixture was refluxed for 1 h to recover the products completely. The solution was made alkaline, filtered, and the organic products were extracted and analyzed by gas chromatography.

3. RESULTS

3.1. N-Methylation of aniline

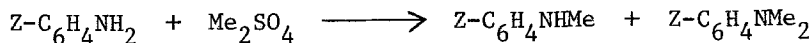


In the presence of alkali cation exchanged Y-type zeolite, the reaction of aniline with dimethyl sulfate was promoted to give N-methylaniline and N,N-dimethylaniline (Table I)[3]. The order of the effectiveness of alkali cation of Y-type zeolite was $\text{K} > \text{Na} > \text{Cs}$ in the conversion. X-Type zeolite also accelerated the reaction.

With regard to the selectivity of N-monomethylation to N,N-di-methylation, KY, CsY, and KX showed good results. Neutral alumina for column chromatography also promoted the reaction, but the selectivity was very low.

Nonpolar solvents like aromatic hydrocarbons can be preferably employed in the present reaction. On the contrary, polar solvents such as tetrahydrofuran and N,N-dimethylformamide retarded the N-alkylation.

3.2. N-Methylation of aniline derivatives



(Z: A substituent group on a benzene ring)

Aniline derivatives such as toluidines, chloroanilines and nitroanilines were methylated in toluene by the treatment with dimethyl sulfate, since the N-methylation of aniline derivatives proceeded in higher selectivity in toluene than in benzene (Table II). Except for *o*- and *p*-nitroaniline, N-methylation was facilitated well by the use of KY.

Table I. N-Methylation of aniline with dimethyl sulfate^{a)}

Additive	Aniline Conv.(%)	PhNHMe	:	PhNMe ₂
None	34	2.2	:	1
NaY	53	2.6	:	1
KY (K ⁺ 99%,Na ⁺ 1%)	71	8.9	:	1
	(58) ^{b)}	(21	:	1) ^{b)}
CsY(Cs ⁺ 68%,K ⁺ 32%)	48	20	:	1
NaX	52	3.0	:	1
KX (K ⁺ 93%,Na ⁺ 7%)	63	12	:	1
Al ₂ O ₃ (neutral) ^{c)}	67	1.2	:	1
Na ₂ CO ₃	66	3.0	:	1

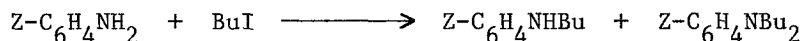
a) PhNH₂(0.5 mmol), Me₂SO₄(0.25 mmol), Zeolite(0.5 g), Na₂CO₃(0.5 g), Alumina(1 g), benzene, reflux, 9 h.

b) KY(1.0 g) was used.

c) Woelm aluminium oxide W-200-neutral, activity grade super I.

[†] As regards the selectivity of N-alkylated products, each isomer of aniline derivatives showed different selectivities. The meta-isomer was inclined to be monoalkylated in higher selectivity compared with the ortho- and para-isomers.

3.3. N-Butylation of aniline derivatives



In contrast to N-methylation with dimethyl sulfate, N-butylation of aniline with butyl iodide scarcely occurred in benzene under reflux conditions without bases. However, the use of KX and KY accelerated the N-butylation to yield N-monobutylaniline exclusively (Table III) [3]. On the contrary, the use of usual inorganic bases like sodium carbonate gave poor selectivity.

o-, *m*- and *p*-Toluidines were also butylated to give the corresponding N-monobutyltoluidines in very high selectivity.

In the case of *m*- and *p*-nitroanilines, only monobutylated products were obtained. In the presence of sodium carbonate or tributylamine, N-butylation did not take place under the same reaction conditions. However, even by the use of KY, *o*-nitroaniline could not be butylated owing to its very low reactivity caused by the strongly electron-withdrawing effect of the *o*-nitro group.

It is noted that zeolite KY promotes *N*-monoalkylation of the aniline derivatives which have very low nucleophilicity.

4. DISCUSSION

The acid site on zeolite is an exchanged cation or a trivalent aluminium atom. The base site is considered to be the SiO⁻ moiety in the lattice (Fig. 1). The acid and base properties of zeolite can be easily altered by the cation exchange.

The acid and base strengths of cation exchanged Y-type zeolite were measured in benzene by the use of the Hammett indicators [4]. The order of maximum acid strength of alkali cation exchanged Y-type zeolites was NaY > KY > CsY, while the order of maximum base strength was CsY > KY > NaY. *N*-Alkylation of amine with an alkylating agent was usually enhanced by the function of base. In the presence of alkali cation exchanged zeolite, the *N*-alkylation of aniline was facilitated in the following order: KY > NaY > CsY. This result was not coincident with the base strength order of the zeolites described above. We supposed that the present *N*-alkylation was prompted by the functions of not only the basic sites on zeolites but also the acidic sites. That is, the basic sites activate the amino group of aniline derivatives and the acidic sites activate the alkylating agent simultaneously (Fig. 1). KY revealed higher activity than NaY and CsY because KY has both the moderately acidic and basic sites suitable for the *N*-alkylation.

Zeolites X and Y have large pores enough to contain an aniline molecule and an alkylating agent. The outer surface area of X and Y zeolites is less than 2% of the inner surface area. Thus it is probable that the *N*-alkylation of aniline derivatives is promoted inside the pore of zeolite. The high selectivity of *N*-monoalkylation appears to be attributed to the stability difference between the transition states (I) and (II) (Fig. 1). Because the transition state (II) is less stable than the transition state (I) due to the steric congestion between the alkyl group (R) and the zeolite cavity, the *N*-alkylation in the state (I) is more facilitated than that in the state (II) to give *N*-monoalkylated products in high selectivity.

In conclusion, potassium cation exchanged X- and Y-type zeolites have very weak acid and base sites, but they are nevertheless found to work as effective promoters in *N*-alkylation of aniline derivatives in nonpolar organic solvent owing to the dual function of the acid and base. The highly selective *N*-monoalkylation is ascribed to the reactions occurring inside the homogeneous narrow pores of zeolites.

Table II. N-Methylation of aniline derivatives with dimethyl sulfate^{a)}

Z	Additive	Time(h)	Conv.(%)	ArNHMe	:	ArNMe ₂
<i>o</i> -Me	None	10	43	3.9	:	1
	KY	10	71 (46) ^{b)}	13	:	1 (2.6 : 1) ^{b)}
	Na ₂ CO ₃	10	42	5.0	:	1
<i>m</i> -Me	None	6	25	2.9	:	1
	KY	6	58 (51) ^{b)}	17	:	1 (10 : 1) ^{b)}
	Na ₂ CO ₃	6	28	4.2	:	1
<i>p</i> -Me	None	9	29	1.8	:	1
	KY	9	68 (31) ^{b)}	5.9	:	1 (3.5 : 1) ^{b)}
	Na ₂ CO ₃	9	43	2.9	:	1
<i>o</i> -Cl	None	9	35	5.9	:	1
	KY	9	63	8.2	:	1
	Na ₂ CO ₃	9	33	5.8	:	1
<i>m</i> -Cl	None	10	44	3.3	:	1
	KY	10	79	12	:	1
	Na ₂ CO ₃	10	49	3.3	:	1
<i>p</i> -Cl	None	12	38	2.2	:	1
	KY	12	74	11	:	1
	Na ₂ CO ₃	12	47	3.9	:	1
<i>o</i> -NO ₂	None	8	2.7	Only ArNHMe		
	KY	8	15	0.4	:	1
	Na ₂ CO ₃	8	4.1	Only ArNHMe		
<i>m</i> -NO ₂	None	8	28	8.0	:	1
	KY	8	71	19	:	1
	Na ₂ CO ₃	8	47	11	:	1
<i>p</i> -NO ₂	None	8	22	4.0	:	1
	KY	8	39	1.9	:	1
	Na ₂ CO ₃	8	30	4.0	:	1

a) ArNH₂(0.5 mmol), Me₂SO₄(0.25 mmol), KY(1 g), Na₂CO₃(1 g), toluene, reflux.

b) benzene, reflux.

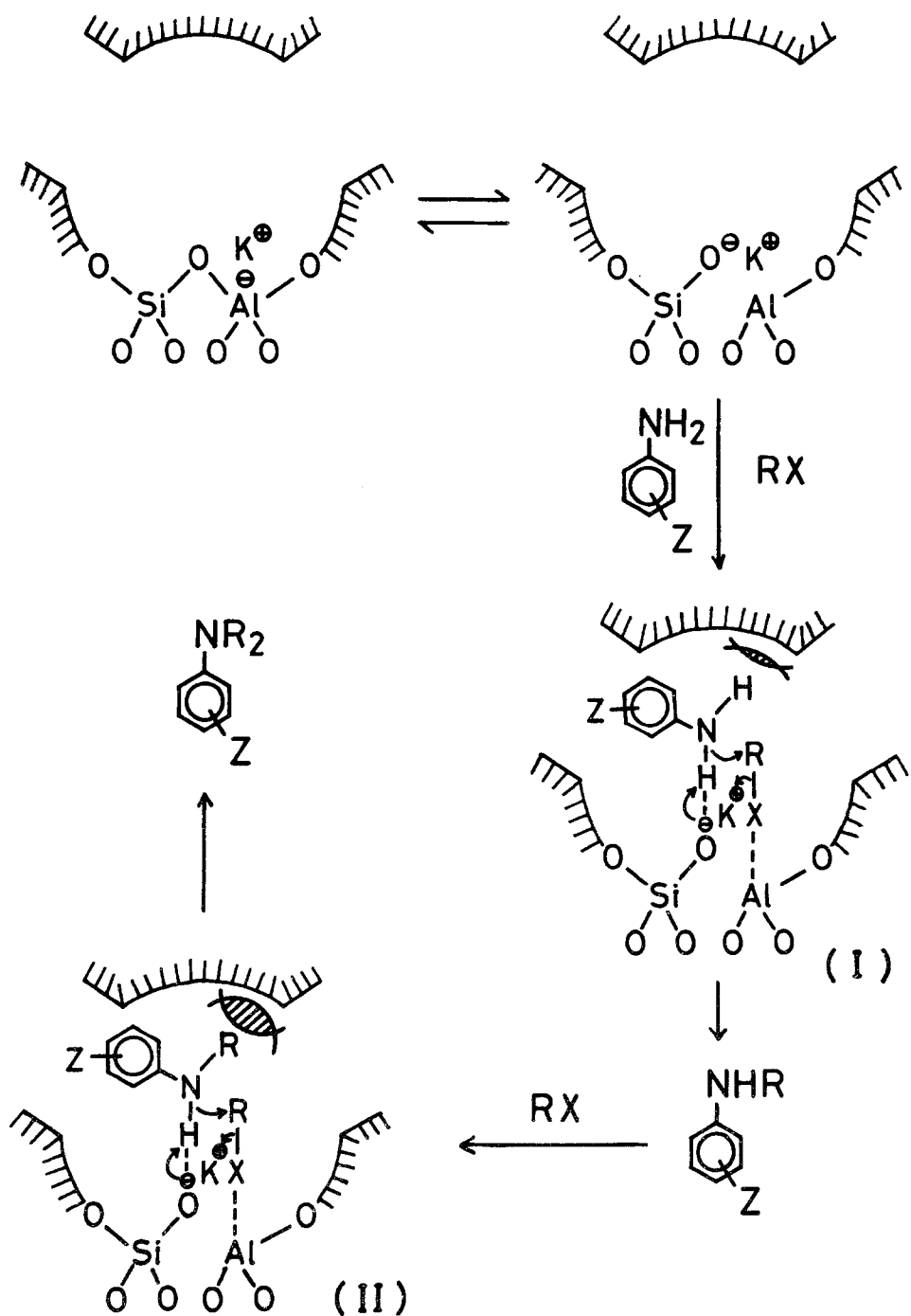
Table III. N-Butylation of aniline derivatives with butyl iodide^{a)}

Z	Additive	Time(h)	Conv.(%)	ArNHBu	:	ArNBu ₂
H	None	23	1.4		—	
	KX(0.5 g)	14	64	74	:	1
	NaX(0.5 g)	14	47	82	:	1
	KY(0.5 g)	14	67	97	:	1
	NaY(0.5 g)	14	58	120	:	1
	Bu ₃ N(1 mmol)	16	26	8.7	:	1
	Na ₂ CO ₃ (0.5 mmol)	5	57 ^{b)}	1.3	:	1
<i>o</i> -Me	None	10	0.6		—	
	KY(1 g)	5	82	300	:	1
	Na ₂ CO ₃ (0.5 g)	5	40 ^{b)}	9.1	:	1
<i>m</i> -Me	None	10	1.5		—	
	KY(1 g)	5	80	96	:	1
	Na ₂ CO ₃ (0.5 g)	5	72 ^{b)}	2.6	:	1
<i>p</i> -Me	None	10	2.1		—	
	KY(1 g)	5	82	75	:	1
	Na ₂ CO ₃ (0.5 g)	5	62 ^{b)}	3.1	:	1
<i>o</i> -NO ₂	None	20	0		—	
	KY(1 g)	5	0.3		—	
	Na ₂ CO ₃ (1 g)	20	0		—	
<i>m</i> -NO ₂	None	20	0		—	
	KY(1 g)	5	55	Only ArNHBu		
	Al ₂ O ₃ (neutral, 1 g)	5	19	Only ArNHBu		
	Bu ₃ N(1.5 mmol)	20	8.7	Only ArNHBu		
	Na ₂ CO ₃ (1 g)	20	0		—	
<i>p</i> -NO ₂	None	20	0		—	
	KY(1 g)	5	55	Only ArNHBu		
	Na ₂ CO ₃ (1 g)	20	0		—	

a) ArNH₂(0.5 mmol), BuI(0.5 mmol), benzene, reflux.

b) Without solvent, at 80 °C.

Fig. 1. The reaction scheme of an aniline derivative and an alkylating agent (RX:alkylating agent)



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