Zeolite-Promoted Benzylation of Alcohols

Makoto Onaka,* Motomitsu Kawai, and Yusuke Izumi
Department of Synthetic Chemistry, Faculty of Engineering, Nagoya University, Furo-cho,
Chikusa-ku, Nagoya 464
(Received January 13, 1986)

Zeolite-promoted benzylation of alcohols with benzyl chloride has been investigated. By use of a series of cation-exchanged zeolites, which have the same crystalline structure but different acid and base properties, it is confirmed that the cooperative function of acid sites and base sites of zeolite is required for the effective benzylation of alcohols although both acid and base strengths are low. It is also found that alcohols show different reactivities in zeolite from those in solution depending on their molecular structures because the benzylation is promoted inside the narrow cavities of zeolite.

Recently heterogeneous organic reactions effected by inorganic porous solids or reagents adsorbed on those solids are attracting much attention to organic chemists because of attainment of high selectivity, mild reaction conditions, and simple operations.[1] However, what a role these porous solids play in promotion of organic reactions is still not completely elucidated.

Among inorganic porous solids we have been particularly concerned with zeolites and applied them to liquid-phase organic reactions.[2] The most remarkable feature of zeolites is that 1) zeolites have rigid and homogeneous crystalline structures (a definite pore size) and 2) acid-base properties of zeolites can be easily altered by exchange of cations in zeolite without any change of the crystalline structure.[3] We applied a series of cation-exchanged zeolites which have different acid and base properties with the same crystalline structure to benzylation of alcohols and investigated the influence of the zeolite properties on the benzylation. We have reported our preliminary results,[4] and this paper presents in detail our results of zeolite-promoted benzylation and a role of zeolite as an activator.

Results and Discussion

Benzylation of alcohols to benzyl ethers is one of familiar methods for protection of hydroxyl groups,[5] and is generally carried out by use of strong bases such as NaH[6] and KOH.[7] New benzylation methods under milder reaction conditions are required. Thus the application of inorganic porous solids to the benzylation of alcohols was examined.

$$\text{ROH} + \text{PhCH}_2\text{Cl} \longrightarrow \text{ROCH}_2\text{Ph} + \text{HCl}$$

The reaction of 1-decanol with an equimolar amount of benzyl chloride was chosen as a model reaction, and investigated in hexane in the presence of various types of inorganic solids such as alkali cation (M^+)-exchanged X and Y type zeolites (abbreviated as MX and MY, respectively) which have uniform cavities (about 13 Å in diameter),[3b] γ-alumina (neutral and basic) for column chromatography, and KF impregnated on γ-alumina (KF/Al_2O_3).[8] The results are summarized in Table 1.

Between the two types of zeolites, zeolite Y was more effective than zeolite X. Especially the use of potassium cation-exchanged Y type zeolite (KY) showed the highest yield (73%) and 23% of the starting alcohol was remained intact.

The zeolite acts not only as a promoter of the benzylation but also as a base which traps the hydrogen chloride evolved during the reaction.

Alumina (neutral and basic) and KF/Al_2O_3 also promoted the reaction. In these cases, however, dibenzyl ether was obtained as a by-product in 5—16% yields. Residual water on the alumina surface easily hydrolyzed benzyl chloride to benzyl alcohol which

Table 1. Benzylation of 1-Decanol with Benzyl Chloride[a)]

Additive	Yield/%[b)]		Recovery/%[b)]
(Amount)	Benzyl decyl ether	Dibenzyl ether	1-Decanol
None	0	0	100
NaY (0.8 g)	15	0	47
KY (0.8 g)	73	0	23
CsY (0.8 g)	62	0	37
NaX (0.8 g)	4	0	86
KX (0.8 g)	8	0	92
Al_2O_3 (neutral, 1.2 g)	41	5	58
Al_2O_3 (basic, 1.2 g)	48	7	52
KF/Al_2O_3 (5.5 mmol)	62	16	20
K_2CO_3 (0.5 g)	0	0	100
Et_3N (1 mmol)	0	0	100

a) Reaction of 1-decanol (1 mmol) with benzyl chloride (1 mmol) and the additive in 5 ml of hexane was carried out under reflux for 5 h. b) Determined by GLC using diphenylmethane as an internal standard.

Table 2. Zeolite KY-Promoted Benzylation of 1-Decanol in Various Solvents

Solvent	Yield/%[b]	Recovery/%[b]
	Benzyl decyl ether	1-Decanol
Hexane	73	23
C_6H_6[c]	42	57
C_6H_5Cl[d]	77	21
CCl_4	77	23
$CHCl_3$	4	95
THF	0	100

a) Reaction of 1-decanol (1 mmol) with benzyl chloride (1 mmol) and KY (0.8 g) was carried out in a solvent under reflux for 5 h. b) Determined by GLC using diphenylmethane as an internal standard. c) Diphenylmethane was obtained in 28% yield as a byproduct. d) Reaction was carried out at 80 °C for 5 h.

Table 3. Acid Strength Distribution of Zeolites and Alumina in Hexane (meq/g)

Porous solid	H_0 $\leqq+1.5$	$\leqq+2.0$	$\leqq+3.3$	$\leqq+4.0$	$\leqq+6.8$
NaY	0.006	0.008	0.012	0.028	0.25
KY	0	0	0.012	0.012	0.052
CsY	0	0	0	0	0.018
NaX	0	0	0	0.77	0.86
KX	0	0	0	0	0
Al_2O_3[a]	0	0	0.009	0.069	0.15

a) Neutral alumina.

Table 4. Base Strength Distribution of Zeolites and Alumina in Hexane (meq/g)

Porous solid	H_0 $\geqq+1.5$	$\geqq+2.0$	$\geqq+3.3$	$\geqq+4.0$	$\geqq+6.8$
NaY	0	0	0	0	0
KY	0.030	0.019	0	0	0
CsY	0.20	0.19	0.012	0.002	0
NaX	0.080	0.080	0.040	0	0
KX	0.93	0.42	0.014	0.003	0.002
Al_2O_3[a]	0.065	0.050	0	0	0

a) Neutral alumina.

Table 5. Zeolite KY-Promoted Benzylation of Various Alcohols[a]

Alcohol	Yield/%[b]	Recovery/%[b]
	Benzyl ether	Unreacted alcohol
Benzyl alcohol	57	33
1-Decanol	73 (84)[c]	23 (15)[c]
1-Octanol	69	24
2-Octanol	51 (61)[d]	25 (15)[d]
4-Octanol	40 (30)[e]	22 (64)[e]

a) Reaction of an alcohol (1 mmol) with benzyl chloride (1 mmol) and zeolite KY (0.8 g) was carried out in hexane under reflux for 5 h. b) Determined by GLC using diphenylmethane as an internal standard. c) Benzyl chloride (1.5 mmol) was used. d) Benzyl chloride (2 mmol) was used. e) Reaction was carried out at r.t. for 100 h.

was in turn benzylated to produce dibenzyl ether. In contrast with alumina, residual water in the zeolites did not cause the side reaction (Table 1).

Bases such as powdered potassium carbonate and triethylamine could not induce the benzylation of 1-decanol in hexane.

In various solvents was studied the benzylation of 1-decanol with zeolite KY as shown in Table 2. Nonpolar solvents such as hexane and carbon tetrachloride were most suitable for the reaction. In benzene was produced diphenylmethane in 28% yield based on benzyl chloride in addition to the benzyl ether. The acid sites of zeolite KY were considered to cause the Friedel–Crafts reaction of benzene with benzyl chloride. When chlorobenzene was employed as a solvent instead of benzene, the Friedel–Crafts reaction was suppressed and the yield of benzyl decyl ether improved.

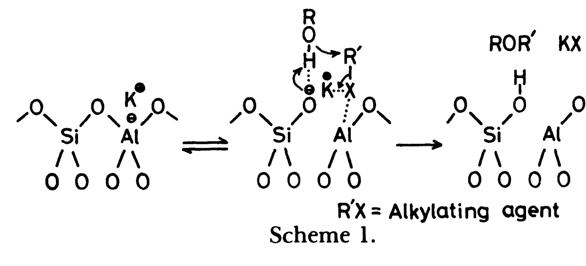
The use of relatively polar solvents like chloroform and tetrahydrofuran (THF) drastically retarded the reaction. THF is relatively basic and hence acid sites of zeolite were neutralized by THF.

It is assumed that the difference of effectiveness in the benzylation between the zeolites was ascribed to those of intrinsic acid and base properties of zeolites. Thus we examined acid and base properties of the zeolites and alumina, and related them to the results of benzylation of 1-decanol.

According to the reported method[9] we measured distribution of acid-base strength of the zeolites and the alumina which were employed in the present study by use of Hammett indicators, butylamine, and trichloroacetic acid.

In the zeolite Y series, the maximum acid strength was in the order of NaY>KY>CsY (Table 3), whereas the maximum base strength was in the order of CsY>KY>NaY (Table 4).

When the effectiveness of the zeolites as a promoter was judged in terms of the yield of benzyl ether, the order was KY>CsY>NaY, which was not consistent with the order of the maximum base strength of the zeolites. This result indicates that the benzylation is not promoted only by a base site of the zeolite, but the cooperative function of an acid site and a base site of the zeolite is necessary for the effective benzylation of alcohols although both acid and base strengths are relatively low. We assume that, in the transition state of benzylation, within a cavity of the zeolite two molecules of an alcohol and benzyl chloride are oriented such a way that nucleophilicity of a hydroxyl group of the alcohol can be enhanced by a base site and benzyl chloride can be activated by an acid site concertedly depicted below.



Scheme 1.

Table 6. Effects of Molecular Size of Alcohols on Benzylation

Alcohol	Method A[a]	Method B[b]
	Yield/%[c] (Relative yield)[e]	Yield/%[d] (Relative yield)[e]
1-Decanol	73 (1)	73 (1)
Benzyl alcohol	57 (0.78)	80 (1.10)
Cyclohexylmethanol	58 (0.79)	80 (1.10)
Neopentyl alcohol	53 (0.73)	77 (1.05)
1-Adamantylmethanol	15 (0.21)	80 (1.10)

a) Method A: Reaction of an alcohol (1 mmol) with benzyl chloride (1 mmol) and zeolite KY (0.8 g) was carried out in hexane under reflux for 5 h. b) Method B; Sodium alkoxide (20 mmol) which was prepared from an alcohol (20 mmol) and NaH (25 mmol) was treated with benzyl bromide (20 mmol) in THF under reflux for 5 h. c) Yield determined by GLC. d) Isolated yield. e) (Yield of corresponding benzyl ether of alcohol)/yield of benzyl decyl ether).

Neutral alumina was found to have analogous acid-base character to zeolite KY. The activity difference between the zeolite KY and the alumina may be attributed to the different mutual location of acid and base sites which is decisive to promote the reaction efficiently.

Table 5 shows the results of the benzylation of various alcohols. In comparison with primary alcohols, secondary alcohols were subject to dehydration and the yields of benzyl ethers decreased.

Zeolite Y consists of uniform cavities (13 Å in diameter) which incorporate various organic molecules and the external surface area of zeolite Y is only 0.5—1.3% of the total surface area.[3a)] In Fig. 1 are shown adsorption isotherms for 1-decanol, cyclohexylmethanol, and 1-adamantylmethanol on zeolite KY in benzene at 30 °C. Bulky alcohols like 1-adamantylmethanol can be adsorbed in the zeolite. Hence in the present benzylation most of alcohols are considered to be adsorbed inside the cavities to undergo benzylation.

The molecular size of an alcohol and the steric bulkiness around a hydroxyl group of the alcohol are expected to influence the reaction rate of benzylation in zeolite. Thus the benzylation of five primary alcohols was studied by use of zeolite KY in comparison with the results obtained by a conventional method (the use of sodium hydride and benzyl bromide in THF) shown in Table 6. The steric hindrance around hydroxyl groups of the alcohols examined was estimated by use of the CPK molecular model in the following order: 1-decanol<benzyl alcohol<cyclohexylmethanol<neopentyl alcohol<1-adamantylmethanol. From the results of the conventional method it was confirmed that the five alcohols have almost the same reactivity in a solution. In the zeolite-promoted benzylation, however, it was observed that the reactivities of the alcohols decreased in the order of 1-decanol>benzyl alcohol≈cyclohexylmethanol≈neopentyl alcohol ≫1-adamantylmethanol. The adsorption isotherms for 1-decanol, cyclohexylmethanol, and 1-adamantylmethanol on zeolite KY in benzene in Fig. 1 show that the adsorption amount of cyclohexylmethanol is larger than those of 1-decanol and 1-adamantylmethanol. This fact means that the benzylation of alcohols inside the zeolite cavities is not governed by the ability of the alcohols to be adsorbed.

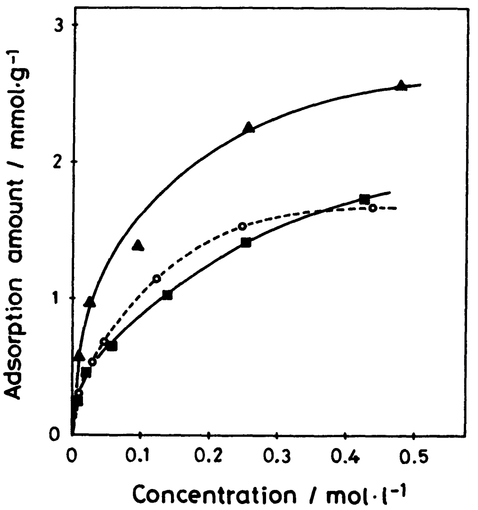


Fig. 1. Adsorption isotherms of alcohols on zeolite KY in benzene at 30 °C: 1-Decanol (○), Cyclohexylmethanol (▲), 1-Adamantylmethanol (■).

Table 7. Zeolite KY-Promoted Alkylation of 1-Octanol with Various Alkylating Agents[a]

R′X	Solvent	Yield of ether/%[b]
$PhCH_2Cl$	Hexane	69
$CH_2{=}CHCH_2Br$	CCl_4	58
$n\text{-}C_6H_{13}I$	Heptane	32
$CH_3OCH_2CH_2OCH_2Cl$	Hexane	0
CH_3SCH_2Cl	Hexane	0

a) Reaction of 1-octanol (1 mmol) with an alkylating agent (1 mmol) was carried out in solvent under reflux for 5 h. b) Isolated yield.

On the basis of the facts described above, we assume that the benzylation is greatly affected by whether the molecules of benzyl chloride and alcohol can be adequately arranged to the acid and base sites (Scheme 1) or not. Thus 1-adamantylmethanol may be too sterically hindered to be oriented in close proximity to a benzyl chloride molecule inside a cavity of zeolite.

In order to survey the limitations of reactions promoted by zeolite were investigated reactions of various

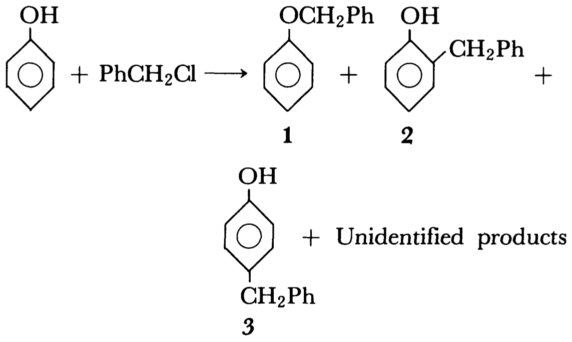
Table 8. Benzylation of Phenol[a)]

Additive	Yields/%[b)] 1	2	3	Recovery of PhOH/%[b)]
KY	12	20	12	43
CsY	24	4	5	66
KX	3	1	0	96
Al_2O_3[c)]	0	42	3	35

a) Reaction of Phenol (1 mmol) with benzyl chloride (1 mmol) and zeolite (0.8 g) or alumina (1.2 g) was carried out in CCl_4 under reflux for 5 h. b) Determined by GLC. c) Neutral alumina.

alkylating agents with alcohols and benzylations of phenolic hydroxyl groups and amino groups. In Table 7 are shown alkylations of alcohols by use of allyl bromide, hexyl iodide, 2-methoxyethoxymethyl chloride, and chloromethyl methyl sulfide.

Benzylation of phenol is expected to occur in two ways: *O*-benzylation and *C*-benzylation (Table 8).



CsY, which is more basic than KY, induced *O*-benzylation more preferably than *C*-benzylation although the yield was low. Interestingly, by use of neutral alumina, *C*-benzylation products were mainly obtained and benzyl phenyl ether was not produced.

Besides alcohols, amines and amides were successfully benzylated to give the corresponding monobenzylation products selectively by use of zeolite KY.

$$PhNH_2 + PhCH_2Cl \xrightarrow[\text{PhH,50°C,5h}]{\text{KY}} PhNHCH_2Ph + PhN(CH_2Ph)_2$$
$$84\,\% \qquad 6\,\%$$

$$CH_3CONH_2 + PhCH_2Cl \xrightarrow[\text{PhCl,80°C,5h}]{\text{KY}} CH_3CONHCH_2Ph \quad 80\,\%$$

Experimental

Materials. Unless otherwise noted, reagents were all commercial ones and used without further purification. THF was dried over sodium benzophenone ketyl. Chlorobenzene was distilled over calcium hydride. Chloroform was passed through a column of neutral alumina. Other solvents were dried over molecular sieve 3A. Zeolite NaX (Union Showa Co.), zeolite NaY (a reference catalyst from the Catalysis Society of Japan: JRC-Z-Y4.8, $SiO_2/Al_2O_3=4.8$), alumina (neutral)(Woelm 200 neutral, activity super I), and alumina (basic)(Woelm 200 basic, activity super I) were used. Potassium ion-exchanged X and Y type zolites were prepared from NaX and NaY according to the ion exchange technique. Preparation of KY from NaY shown as a typical example is as follows: Powdered zeolite NaY (100 g) was immersed in an aqueous 0.5 M (1 M=1 mol dm^{-3}) KCl solution (1000 ml) at 70 °C for 3 h with occasional stirring, and the zeolite was filtered on a Buchner funnel. This procedure was repeated 10 times. The ion-exchanged zeolite was washed with deionized water until no chloride ion could be detected in the washings by use of $AgNO_3$, dried at 110 °C for 12 h, and kept in a desiccator. Cesium ion-exchanged zeolite Y (CsY) was prepared by treatment of KY with an aqueous CsCl solution in the similar manner to that described above. The content of cations in zeolites was determined by atomic absorption analysis: NaX (Na^+ 100%), KX (K^+ 93%, Na^+ 7%), NaY (Na^+ 100%), KY (K^+ 99%, Na^+ 1%), and CsY (Cs^+ 68%, K^+ 32%). Zeolite and alumina were dried again at 500 °C for 5 h prior to the use. The activities of the zeolites and the aluminas remained unchanged after a few weeks' storage in a desiccator.

The KF impregnated on Al_2O_3 (Merck 90 neutral, Art. 1077) reagent was prepared according to the method reported by Ando et al.[8)]

All zeolites and aluminas were handled in the atmosphere as quickly as possible.

Analysis. GLC analyses were performed by a Shimadzu GC-8A gas chromatograph with columns (10% Silicone SE30 (Uniport B), 25% Silicone DC550 (Uniport B), and 10% PEG20M (Uniport B)), a flame ionization detector and a System Instruments 5000E integrator.

All the reaction products were identified as being identical with authentic samples. Yields of the products and recoveries of the starting materials were determined by GLC using internal standards unless otherwise mentioned.

Reaction Procedure. Use of Zeolite and Alumina: In a flask were placed zeolite (0.8 g)(or alumina (1.2 g)) and solvent (2 ml) under nitrogen. To the flask was added a solution of an alcohol (1 mmol) and an alkylating agent (1 mmol) in solvent (3 ml), and the suspended mixture was allowed to be stirred under the conditions shown in Tables. As work-up, water (3 ml) was added, and the resulting mixture was heated under reflux for 0.5 h. This work-up procedure is necessary in order to extract organic products in the zeolite completely. After the mixture was cooled, the zeolite was filtered off and organic products were extracted with ethyl acetate from the filtrate. The extract was dried over sodium sulfate, filtered and analyzed.

Use of NaH: To a suspension of sodium hydride (25 mmol) in 15 ml of THF under nitrogen at 0 °C was dropwise introduced a solution of an alcohol (20 mmol) in 15 ml of THF. The mixture was stirred at 50 °C for 1 h. To it was added a solution of benzyl bromide (20 mmol) in 15 ml of THF at 0 °C. The mixture was allowed to be stirred under reflux for 5 h. After the flask was cooled to 0 °C, excess 1 M HCl solution was added to quench the reaction. The organic layer was extracted with ethyl acetate, dried over sodium sulfate, filtered, and concentrated in vacuo. Distillation of the residue afforded benzyl ether.

Measurement of the Distribution of Acid and Base Strength. According to the literature,[9)] we measured acid-base properties of zeolites and aluminas which were applied to the present study. The acid strengths and amounts of a solid were measured by titrating the solid suspended in hexane with a solution of butylamine in hexane using Hammett indicators (pK_a value): 4-phenylazo-*N*-phenylaniline (+1.5), 4′-amino-2,3′-dimethylazobenzene (+2.0), 4-dimethylaminoazobenzene (+3.3), 4-phenylazo-1-naphthylamine (+4.0), and Neutral Red (+6.8). The base strengths and amounts of a solid were measured by titrating the solid suspended in hexane with a solution of trichloroacetic acid in hexane using the same indicators as those listed above.

The authors thank Professors Yuichi Murakami and Tadashi Hattori and Drs. Miki Niwa and Hirofumi Itoh of Nagoya University for helpful advice concerning zeolites. They also thank Dr. Kuniyuki Kitagawa of Nagoya University for advising atomic absorption analyses.

References

1) a) G. H. Posner, *Angew. Chem., Int. Ed. Engl.*, **17**, 487 (1978); b) A. McKillop and D. W. Young, *Synthesis*, **1979**, 401, 481; c) M. Hojo and R. Masuda, *Yuki Gosei Kagaku Kyokai Shi*, **37**, 557, 689 (1979); M. Hojo, *ibid.*, **42**, 635 (1984).

2) M. Onaka, K. Ishikawa, and Y. Izumi, *Chem. Lett.*, **1982**, 1783; M. Onaka and Y. Izumi, *ibid.*, **1984**, 2007; M. Onaka, K. Ishikawa, and Y. Izumi, *J. Inclusion Phenomena*, **2**, 359 (1984); M. Onaka, M. Kawai, and Y. Izumi, *Chem. Lett.*, **1985**, 779; M. Onaka, A. Umezono, M. Kawai, and Y. Izumi, *J. Chem. Soc., Chem. Commun.*, **1985**, 1202; M. Onaka, H. Kita, and Y. Izumi, *Chem. Lett.*, **1985**, 1895.

3) a) P. B. Venuto and P. S. Landis, "Advances in Catalysis," ed by D. D. Eley, H. Pines, and P. B. Weisz, Academic Press, New York (1968), Vol. 18, p. 259; b) D. W. Breck, "Zeolite Molecular Sieves," John Wiley & Sons, New York (1974); c) "Zeolite Chemistry and Catalysis," ed by J. A. Rabo, American Chemical Society, Washigton, D. C. (1976).

4) M. Onaka, M. Kawai, and Y. Izumi, *Chem. Lett.*, **1983**, 1101.

5) J. F. W. McOmie, "Protective Groups in Organic Chemistry," Plenum Press, New York (1973), p. 95.

6) a) J. S. Brimacombe, D. Portsmouth, and M. Stacey, *J. Chem. Soc.*, **1964**, 5614; b) T. Iwashige and H. Saeki, *Chem. Pharm. Bull.*, **15**, 1803 (1967); c) S. Czernecki, C. Georgoulis, and C. Provelenghiou, *Tetrahedron Lett.*, **1976**, 3535.

7) H. G. Fletcher, *Methods Carbohydr. Chem.*, **2**, 166 (1963).

8) T. Ando, J. Yamawaki, T. Kawate, S. Sumi, and T. Hanafusa, *Bull. Chem. Soc., Jpn.*, **55**, 2504 (1982).

9) T. Yamanaka and K. Tanabe, *J. Phys. Chem.*, **79**, 2409 (1975).