HETEROGENEOUS CATALYSTS IN THE ALKYLATION OF IMIDAZOLES

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The reaction of imidazoles with alcohols at 300-400°C was studied in the presence of heterogeneous γ -Al₂O₃ catalysts and Y zeolites. The major reaction was found to be N-alkylation. This reaction is accompanied by C-alkylation on γ -Al₂O₃, while the selectivity relative to N-alkylation is close to 100% on zeolite catalysts. The greatest activity with 100% selectivity was found for H zeolite. The alkylation of methanol and ethanol by 2-methylimidazole at 310-320°C gave 1,2-dimethylimidazole in ~100% yield and 1-ethyl-2-methylimidazole in 90% yield respectively. The reaction of methanol and imidazole gave 1-methylimidazole in 99% yield. This catalyst displays high stability and capacity for oxidative regeneration.

N-Substituted imidazoles are used in organic synthesis as catalysts for the acetylation of alcohols [1, 2], phosphorylation of alcohols and amines [3, 4], in the synthesis of oligonucleotides [5, 6], as accelerators for the hardening of epoxy resins in the manufacture of air-tight integral systems [7, 8], in the production of porous polyurethane materials [9], and in the manufacture of several types of textile dyes [10]. The classical method for the preparation of N-alkylimidazoles is the alkylation of imidazoles by alkyl halides in alkaline media [11]. Catalytic methods for N-alkylation using free or supported acids as catalysts have also been described [10, 12, 13].

We have attempted to use heterogeneous acid catalysts, in particular, synthetic zeolites for the alkylation of imidazoles. Synthetic zeolites long been employed for the alkylation of aromatic hydrocarbons by olefins and alcohols and are used in large amounts in Russian industry. The effect of the zeolite structure and the type of exchanged cation has been studied extensively and optimal reaction conditions have been determined [14-19]. This reaction proceeds at 200-350°C. The best mole ratio of the alkylating agent to the aromatic hydrocarbon is in the range from 1:3 to 1:9. The alkylating activity increases with increasing polarizing action of the cation and is greatest for the H form. Alcohols alkylate olefins more completely under identical conditions. For example, the yield of ethylbenzene from benzene and ethylene at 400°C on CaY zeolite is 44%, while the same yield is obtained from ethanol and benzene at only 325°C [17]. Extension of the side chain also occurs in the alkylation of toluene and other alkylbenzenes along with alkylation in the aromatic ring [16] and the yield of products alkylated in the side chain increases with increasing basicity of the exchanged cation. For example, styrene and ethylbenzene comprise 85% of the total reaction products on zeolite RbNaX at 425°C when the methanol conversion is 12%. Thus, there is a very clear effect of the cation on the direction and extent of alkylation of aromatic hydrocarbons.

Imidazoles may give alkyl derivatives by reaction at $C_{(2)}$, C_4), and $C_{(5)}$ or at $N_{(1)}$.



Furthermore, extension of the side chain is possible when there is an alkyl substituent and this may be an alternative for the synthesis of several C-alkylimidazoles difficult to prepare. Zeolites have not yet been used for imidazole alkylation

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Catalyst	<i>Т, °</i> С	Conversion of 2-methy- limidazole, mole, %	Conversion of 2-methy- limidazole, mole, %	Catalyst	<i>T</i> . °C	Selectivity relative to - 1,2-dimethy- limidazole, mole, %	Selectivity relative to 1,2-dimethy- limidazole, mole, %
γ-Λl2O3	350 400	92,5 100	91,0 78,0	NaY	300 350 400	25,0 60,5 84,5	100 100 97,5
ΛΙ2Ο3— 2% K2O	350 400	60,5 93,0	98,0 93,5	RbNaY	350 400 450	75,6 96,1 100	100 99,0 90,0
Al2O3— 2% Rb2O	350 400 450	54,8 88,7 98,8	98,8 96,2 86,2	HNaY	300 350	100 100	100 100

TABLE 1. Alkylation of 2-Methylimidazole by Methanol in the Presence of Zeolite Y and γ -Al₂O₃ Catalysts^{*}

*The mole ratio of methanol to 2-methylimidazole was 3.2:1 and the volumetric rate for passage of the solution was $0.7 h^{-1}$.

although their use in the alkylation of thiophene, pyrrole, and furan has been reported [15]. Thus, we studied the feasibility of the heterogeneous catalytic alkylation of imidazoles, determined the course of the alkylation pathway, and checked the effect of the introduced cation on the activity and selectivity of the catalyst in this reaction. Zeolite Y and γ -Al₂O₃ catalysts were used. The Na form of zeolite Y as well as the Rb⁺, Cs⁺, and H forms obtained by ion exchange from NaY were studied. The acidity of the γ -Al₂O₃ support was controlled by the introduction of alkaline additives such as K₂O and Rb₂O. The reaction of methanol with 2-methylimidazole (I), in which all three alkylation pathways indicated above are possible, was taken as the model reaction.

1,2-Dimethylimidazole (Ia) is the major product in the reaction of I with methanol on γ -Al₂O₃, i.e., 2-methylimidazole is alkylated predominantly at nitrogen. The products of the alkylation of I at carbon are formed in addition to I, including 1,2,4-trimethylimidazole, 1,2,4,5-tetramethylimidazole, and some other unidentified compounds. Table 1 shows that the selectivity relative to Ia at 350°C, that is, the ratio of the yield of Ia to the total conversion of I, is 91%. The selectivity relative to Ia drops to 78% at 400°C when the conversion reaches 100%. The selectivity characterizing the alkylation of methanol is much lower and does not exceed 50%, indicating loss of a portion of the methanol in side reactions such as the formation of dimethyl ether and gaseous hydrocarbons. The addition of K₂O and Rb₂O, which does not have a fundamental effect on the nature of these transformations, reduces the conversion of I but somewhat increases the selectivity relative to Ia at equal conversions.

Zeolites proved more efficient in the alkylation of 2-methylimidazole. The selectivity relative to Ia for the initial Na form is close to 100% at 300-350°C although the conversion of I did not exceed 60%. The conversion of I increased to 84.5% at 400°C with some loss of selectivity. RbNaY proved the most active (76-100% conversion) but less selective in the alkylation of I. Extension of the side chain, as described for the alkylation of toluene [16], was not observed. The H form of zeolite Y held the greatest interest. The conversion of I reached 100% on this catalyst even at 300-310°C with almost 100% selectivity. Methanol was consumed virtually only in the formation of 1,2-dimethylimidazole, that is, the selectivity of methanol relative to alkylation is also close to 100%.

Zeolite HNaY was checked for stability in the alkylation of 2-methylimidazole by methanol. Figure 1 shows that the conversion of I at $310 \pm 6^{\circ}$ C after 16 h did not drop below 99%, while the selectivity remained virtually at 100%. The catalyst was subjected to oxidative regeneration using air at 550°C over 8 h in order to burn off tarry deposits. Figure 1 shows that the conversion in a repeat experiment remained at 99.8% after 6 h with retention of 100% selectivity.

Table 2 shows the results of experiments on the preparation of some other N-alkylimidazoles. The conversion of unsubstituted imidazole (II) by methanol over the entire experiment remained at 100% while the selectivity relative to 1-methylimidazole (IIa) was below 100%. On the other hand, 100% selectivity relative to the formation of 1-ethyl-2-methylimidazole (Ib) was maintained during the entire experiment in the alkylation of 2-methylimidazole by ethanol. The conversion of I in this case was 91% at the very onset and dropped after 3 h to 79% and increased to the initial values only upon raising the temperature to 330° C.

TABLE 2.	Synthesis o	f Several I	N-Alkylimidaz	oles by t	he Alk	ylation (of In	nidazoles
with Alcoho	ols in the Pr	esence of	Zeolite HNaY	*				

Imidazole synthesized	Starting compounds	Time from Reaction onset, h	Imidazole conversion, mole %	Selectivity relative to alkylimidazole, mole %
1,2-Dimethy_ limidazole 1-Methylimi- dazole	2-Methylimidazole, methanol Imidazole, methanol	02 24 46 02 24	100 100 100 100 100	100 100 100 100 99,2
1-Ethyl-2-me- thylimidazole	2-Methylimidazole, ethanol	46 02 24 46	100 91 79 91* ²	99,0 100 100 100 2

*At 310°C, the volumetric rate of the solution of imidazole in alcohol was 0.7 h^{-1} , the alcohol—imidazole mole ratio ranged from 3:1 to 4:1. *²At 330°C.



Fig. 1. Change in the conversion (1) of 2-methylimidazole and selectivity (2) relative to 1,2-dimethylimidazole during the alkylation of 2-methylimidazole by methanol at 310°C. The volumetric inlet rate of the imidazole–alcohol mixture was 0.7 h^{-1} and the methanol–2-methylimidazole mole ratio was 3:1.

Thus, the decationized zeolite Y (HY) proved efficient for the N-alkylation of imidazoles. The alkylation on both zeolite and γ -Al₂O₃ proceeds through an acidic mechanism:

Various types of interaction of imidazole with the surface are likely on γ -Al₂O₃, which has a very broad range of acid sites differing in strength, including one-point, two-point, and planar interaction. This leads to the formation of polyalkylated products. On the other hand, there is probably definite orientation of the basic imidazole nitrogen atom relative to the acid site and subsequent alkylation of imidazoles relative to aromatic hydrocarbons. The selectivity does not fall below 90% even in the case of a three- or four-fold excess of alcohol, while such a large excess of the aromatic hydrocarbon is required in the alkylation of benzene to retain the same selectivity.

EXPERIMENTAL

Catalyst Preparation. An industrial sample of zeolite NaY was used $(Na_2O \cdot Al_2O_3 \cdot 4.8SiO_2 \cdot 8.9H_2O, SiO_2/Al2O_3 = 5.74)$. The Rb⁺, Cs⁺, and H forms were obtained from NaY by ion exchange from solutions of the corresponding salts containing a triple amount of the exchanged ion in comparison with the sodium ion in the starting zeolite. In particular, the H form of zeolite Y was prepared by placing 90 cm³ (56.3 g) zeolite NaY into a 2-liter flask and pouring into 1800 ml of an aqueous solution containing 31.14 g NH₄Cl. The contents were stirred for 6 h on a steam bath. After

standing, the suspension was decanted and the precipitate washed on a glass filter with distilled water until chloride ion was no longer detected in the wash water. This operation was repeated twice. The washed precipitate was dried at 120°C and then roasted for 6 h at 500°C in a muffle furnace. After roasting, the zeolite sample was again subjected to decationization with the same amount of aqueous NH_4Cl and then filtered. The washed precipitate was finally dried and roasted analogously. The powder obtained was pressed and the 1-2-mm fraction was isolated. The extent of decationization was close to 90%.

Samples of A-64 chloride-free alumina (220 m²/g specific surface) were prepared by impregnation of 1-2-mm particles with aqueous solutions containing the calculated amounts of KOH or RbOH. The samples were then dried at 140°C and roasted in an air stream for 4 h at 550°C.

Alkylation Procedure. The alkylation was carried out in a flow unit with a vertical quartz reactor within a block electrical furnace. The solution of the imidazole in alcohol was introduced with a pump and the reaction mixture was collected in cooled traps. The experiments were carried out at 300-400°C and volumetric inlet rates of the imidazole solution of 0.7 h^{-1} . The alcohol – imidazole mole ratio varied from 3:1 to 4:1. The pure product was isolated by initially distilling off the methanol and water. At the conclusion of the distillation, benzene was added to remove traces of water as an azeotrope. The reaction mixture was distilled in vacuum, taking the fraction of the corresponding N-alkylimidazole.

The reaction mixtures were analyzed by gas-liquid chromatography using a 25-m glass capillary column wetted with BSVD copolymer at 190°C. The polyalkylated imidazoles were identified by GC/MS.

1,2-Dimethylimidazole was obtained in 83% yield, bp 99-101°C (21 mm Hg). (bp 204.5°C (760 mm Hg) [10]).

1-Methylimidazole was obtained in 80% yield, bp 94-95°C (24-25 mm Hg). (bp 193°C (760 mm Hg) [10]).

1-Ethyl-2-methylimidazole was obtained in 77.5% yield, bp 98-102°C (16-18mmHg). (bp 110-112°C (22 mm Hg) [10]).

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