

MECHANISTIC STUDIES OF THE PATHWAYS LEADING TO ETHERS *via* COUPLING OF ALCOHOLS

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ABSTRACT

The reaction mechanisms for the solid acid-catalyzed dehydrative coupling of methanol and ethanol with isobutanol and 2-pentanol to form ethers were examined by using isotope labelling and chiral inversion experiments. When the reactions were carried out at 110°C and 1 MPa with ^{18}O -ethanol and ^{16}O -isobutanol over the Amberlyst-35 resin catalyst, 95% of the major product ethyl isobutyl ether (EIBE) contained ^{16}O , while 96% of the minor product ethyl tertiarybutyl ether (ETBE) contained ^{18}O . Similar results were obtained with methanol and isobutanol over Nafion-H and Amberlyst-35 catalysts, with methyl isobutyl ether (MIBE) and methyl tertiarybutyl ether (MTBE) as the products. These results indicate that EIBE (MIBE) was produced by a surface-catalyzed S_N2 reaction, while the ETBE (MTBE) product arose *via* a carbenium intermediate. The analogous reaction carried out over Nafion-H and HZSM-5 catalysts with chiral 2-pentanol verified the surface-mediated S_N2 reaction, wherein chiral inversion of the product ether was observed relative to the S- and R-2-pentanol reactants. In addition, a remarkable shape selectivity with chiral inversion was observed over the HZSM-5 zeolite to selectively form 2-ethoxypentane but not 3-ethoxypentane.

INTRODUCTION

The dehydrative coupling of alcohols to form ethers is practiced on an industrial scale for symmetric ethers with small alkyl groups. In solution phase with an acid catalyst such as H_2SO_4 , it is generally believed that the synthesis of ethers from secondary and tertiary alcohols follow the S_N1 pattern, while synthesis from primary alcohols follow the S_N2 pathway [1]. Mechanistic studies of alcohol dehydration over solid oxide acid catalysts to form olefins and ethers *via* a consecutive-parallel pathway was reported by Knozinger et al. [2]. A series of studies on butanol dehydration over the HZSM-5 catalyst was performed by Makarova et al. [3,4], and ether formation was proposed to proceed *via* a surface- $\text{O}-\text{C}_4\text{H}_9$ intermediate.

Recently, we have explored some possible new routes for synthesizing high value oxygenates, e.g. fuel-grade C_3 to C_6 ethers such as MIBE, MTBE, EIBE, ETBE, ethyl isopropylether (EiPE) and diisopropylether (DiPE), from non-petroleum feed stocks [5-7] owing to the potential use of these ethers as effective anti-knock replacements for leaded gasoline. The $\text{CH}_3^{18}\text{OH}$ /isobutanol coupling reaction over the Nafion-H catalyst was studied, and a S_N2 reaction mechanism was suggested for the production of MIBE [6]. The present work extends the mechanistic study to other alcohol reactants, e.g. ethanol, isopropanol, and chiral 2-pentanol, as well as other solid acid catalysts, i.e. Amberlyst-35 and HZSM-5, and provided additional more generalized mechanistic features of the solid acid-catalyzed ether formation from the corresponding alcohols, $\text{ROH} + \text{R}'\text{OH} \rightarrow \text{ROR}' + \text{H}_2\text{O}$. Experiments were carried out using reactant mixtures in which one of the alcohols (i) was isotopically labelled with ^{18}O or (ii) contained a chiral center.

EXPERIMENTAL

The solid acid catalysts employed in the present study were the commercial Nafion-H with 0.9 meq H^+ /g, Amberlyst-35 from Rohm and Haas with 5.2 meq H^+ /g, and HZSM-5 from Mobil Corporation with a Si/Al ratio of 32/1. The ^{18}O -MeOH and ^{18}O -EtOH reagents with greater than 97% ^{18}O content were purchased from MSD Isotopes. The S-2-pentanol and R-2-pentanol were purchased from Aldrich Chemicals. The experiments were carried out at 90-110°C and 1 MPa total pressure in a gas phase downflow stainless steel tubular reactor with on-line GC analysis of reactants and products to determine alcohol conversion and product selectivities. Typically, the reactant feed contained 3.6 ml/hr liquid alcohol mixture, 88 ml/min He and 12 ml/min N_2 , where the reactant conversion was limited to less than 5%. The liquid products were trapped in a glass cold trap cooled with liquid nitrogen and examined for the source of the ether oxygen by GC/MS and for chirality by a Chirasil-CD column of fused silica column coated with beta-cyclodextrin. The reference compound R-2-ethoxypentane was prepared by using the Williamson synthesis method starting with R-2-pentanol and sodium metal. For comparison, the chiral experiment was also carried out in liquid phase at 100°C and ambient pressure for 1 hr with concentrated H_2SO_4 as the catalyst and the molar ratio of ethanol/2-pentanol/ H_2SO_4 = 4.0/1.0/0.4.

RESULTS

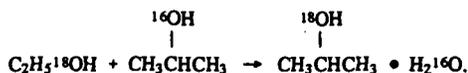
Isotope Labelling Studies of Ether Formation Over Amberlyst-35 Catalyst. The reactants in four experiments where the incorporation of the labelled oxygen into the ether products was monitored were the following:

1. $\text{CH}_3^{18}\text{OH} + (\text{CH}_3)_2\text{CHCH}_2^{16}\text{OH}$
2. $\text{CH}_3\text{CH}_2^{18}\text{OH} + (\text{CH}_3)_2\text{CHCH}_2^{16}\text{OH}$
3. $\text{CH}_3^{18}\text{OH} + \text{CH}_3\text{CH}_2^{16}\text{OH}$
4. $\text{CH}_3\text{CH}_2^{18}\text{OH} + (\text{CH}_3)_2\text{CH}^{16}\text{OH}$.

The labelling results involving isobutanol as a reactant over the Amberlyst-35 catalyst, shown in Tables 1 and 2, were similar to those for the coupling of $\text{CH}_3^{18}\text{OH}$ /isobutanol over the Nafion-H catalyst where the reactions were carried out at 90°C and ambient pressure [6]. In particular, DME (Table 1) and DEE (Table 2) contained almost only ^{18}O , indicating that no oxygen scrambling occurred with the acid catalyst, while MIBE and EIBE retained the ^{16}O of the isobutanol. MIBE and EIBE appear to be formed by the isobutanol attacking the acid-activated methanol and ethanol, respectively, while the methanol and ethanol attacking the isobutanol might be steric hindered. MTBE and ETBE contained ^{18}O , suggesting that these ethers were formed by the coupling of isobutene and the corresponding light alcohols. The isotope distributions in the products are not sensitive to the reaction conditions, e.g. temperature, pressure and relative concentration of the reactant alcohols, nor to the particular resin catalyst employed.

In contrast, the $\text{CH}_3^{18}\text{OH}/\text{CH}_3\text{CH}_2^{16}\text{OH}$ experiment showed that there was no steric (or other) preference in the coupling reaction over Amberlyst-35, and ^{16}O and ^{18}O were found with equal abundance in methyl ethylether (MEE) (Table 3). Again, the isotopic composition of DME and DEE demonstrated that no oxygen scrambling occurred.

In the experiment with ^{18}O -ethanol and ^{16}O -isopropanol (a secondary alcohol), with a 1.0/1.5 molar ratio respectively, the observed products were DIPE, propene, EIPE and DEE, given in order of decreasing selectivity. The isotopic distributions shown in Table 4 clearly showed that the mixed ether EIPE was formed via a mechanism wherein the ^{18}O from the ethanol was retained, while the ^{16}O of the reactant isopropanol molecule was predominantly lost, i.e.



These mechanistic studies utilizing $\text{CH}_3^{18}\text{OH}$ and $\text{CH}_3\text{CH}_2^{18}\text{OH}$ to couple with higher alcohols over the resin catalysts, Nafion-H and Amberlyst-35, indicated that ether synthesis proceeds mainly via a $\text{S}_{\text{N}}2$ reaction pathway to form methyl and ethyl ethers.

Ether Formation From Ethanol and Chiral 2-Pentanol. The definitive proof of a $\text{S}_{\text{N}}2$ reaction mechanism is the observation of the configuration inversion of the product with respect to the reactant. The experiments were carried out with S- or R-2-pentanol and $\text{CH}_3\text{CH}_2^{18}\text{OH}$ over the Nafion-H and HZSM-5 catalysts under the reaction conditions similar to those utilized in the previously described isotope labelling experiments.

The dehydrative coupling of ^{18}O -ethanol and S-2-pentanol produced self-coupling products DEE and di-2-amylether (D2AE), cross-coupling products 2-ethoxypentane (2-EP) and 3-ethoxypentane (3-EP), and the dehydration product 2-pentene but not ethene. The ^{18}O content and chirality of the cross-coupling products are presented in Table 5. For the acid-catalyzed cross-coupling of EtOH and 2-pentanol, the product 2-ethoxypentane can, in principle, be formed either by EtOH attacking the activated 2-pentanol or vice versa. The experiment with Et ^{18}OH was designed to determine the contributions from these two distinct routes. Data in Table 5 demonstrated that the EtOH attack of the acid activated 2-pentanol was the predominant pathway where ^{18}O was retained in the product ether. The true configuration inversion for the ether formation due to EtOH attack of the activated 2-pentanol is given in the last column of Table 5.

The combined ^{18}O retention and the R-/S- chirality results demonstrate that the axial rear-attack $\text{S}_{\text{N}}2$ mechanism dominates (97% over HZSM-5 and 77% over Nafion-H) in this heterogeneous acid-catalyzed dehydrative coupling of alcohols. It is probably due to the steric hindrance that HZSM-5 produced remarkably higher configuration inversion than either the Nafion-H and the H_2SO_4 . The Nafion-H resin catalyst behaved like an acid solution, possibly due to its flexible backbone of the acid groups. The OH group of 2-pentanol is the preferred leaving group, after being activated by the surface H^+ and subjected to the concerted nucleophilic attack by the light alcohol.

The minor paths (23% over Nafion-H and 3% over HZSM-5) can be accounted for by a less efficient carbenium ion (C⁺) or olefin (C⁻) intermediate mechanism. These minor paths are corroborated by observations of the 3-ethoxypentane product, which could only be formed via carbenium ion or olefinic intermediates, over Nafion-H. However, 3-ethoxypentane was not observed as a product with the HZSM-5 catalyst, indicating that the formation of 3-ethoxypentane could be further minimized by shape selectivity in the zeolite pore. The 3-ethoxypentane is more branched and is expected to pass through the HZSM-5 channel (0.55 nm) [8] at a slower rate than 2-ethoxypentane, even if it were formed by the carbenium ion or the olefin reactions at channel intersections.

CONCLUSIONS

The solid acid, Nafion-H, Amberlyst-35 and HZSM-5 zeolite, catalyzed direct coupling of alcohols to form ethers proceeds primarily through a surface-mediated S_N2 reaction pathway that is far more efficient than either a carbenium or olefin pathway. The surface-S_N2 reaction gives rise to high selectivity to configurationally inverted chiral ethers when chiral alcohols were used. This is especially observed in the case of the HZSM-5 catalyst, in which the minor C⁺ or C⁻ paths were further suppressed by "bottling" of 3-ethoxypentane by the narrow zeolite channels.

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Table 1. Percent isotopic composition ($\pm 2\%$) of O-containing products from the reaction of CH₃¹⁸OH/¹⁶O-isobutanol over Amberlyst-35 catalyst at 110°C and 1 MPa.

Isotope	MIBE	MTBE	DME
¹⁸ O	2	93	94
¹⁶ O	98	7	6

Table 2. Percent isotopic composition ($\pm 2\%$) of O-containing products from the reaction of CH₃CH₂¹⁸OH/¹⁶O-isobutanol over Amberlyst-35 catalyst at 110°C and 1 MPa.

Isotope	EIBE	ETBE	DEE
¹⁸ O	<5	96	>93
¹⁶ O	>95	4	<7

Table 3. Percent isotopic composition ($\pm 2\%$) of O-containing products from the reaction of $\text{CH}_3^{18}\text{OH}/\text{CH}_3\text{CH}_2^{16}\text{OH}$ over Amberlyst-35 catalyst at 110°C and 1 MPa.

Isotope	DME	DEE	MEE
^{18}O	<98	<2	50
^{16}O	>2	>98	50

Table 4. Percent isotopic composition ($\pm 2\%$) of O-containing products from the reaction of $\text{CH}_3\text{CH}_2^{18}\text{OH}/^{16}\text{O}$ -isopropanol over Amberlyst-35 catalyst at 90°C and 1 MPa.

Isotope	EIBE	ETBE	DEE
^{18}O	89	<2	>98
^{16}O	11	>98	<2

Table 5. Product selectivities ($\pm 2\%$) (taking into account 2- and 3-ethoxypentane only) from the reaction of Et^{18}OH and S-2-pentanol over Nafion-H and HZSM-5 catalysts at 100°C and 1 MPa, and in concentrated H_2SO_4 solution at 100°C and ambient pressure, where the true inversion = $\%X/(X+Y-Z)$.

Acid Catalyst	Product selectivity (%)			Ratio for R-2-EP/S-2-EP (X/Y)	$^{16}\text{O}/(^{16}\text{O}+^{18}\text{O})$ % in 2-EP (Z)	Inversion (%)
	S-2-EP	R-2-EP	3-EP			
HZSM-5	14.0	86.0	0.0	86/14	11.0	97
Nafion-H	32.9	60.9	6.2	65/35	16.0	77
H_2SO_4	33.6	64.0	2.4	66/34	18.0	80